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AMERICAN MEDICAL ASSOCIATION BULLETIN
Facing page 50

A.M.A. SESSION • ATLANTIC CITY, N. J. • JUNE 7-11, 1937

A Symposium on Metabolic Diseases

The January Number of the "Medical Clinics of North America" (from Chicago) brings to subscribers *25 clinics,* six of them constituting a *Symposium on Metabolic Diseases.* This Symposium includes Gout, Prevention of Diabetic Coma, Obesity, Malnutrition in General Practice, Vitamins in Children's Diets, and Inanition. These certainly are problems of treatment and management that come frequently into the practice of the family physician. That is why these clinics are so successful, that is why they *sell out of print month after month,* notwithstanding the fact that the number of copies printed is consistently increased to meet anticipated demand. The "Medical Clinics of North America" reflect the demands of today's practice!

Then in addition to this Symposium, this January Number alone contains *19 other clinics* on subjects of unusual interest, such as leukemia in childhood, food allergy, pollinosis, duodenal stasis, pneumonia in children, chronic leg ulcers, persistent vaginal discharge, and many others.

The "Medical Clinics of North America" are *books of Clinical Medicine*—not magazines or journals. They bring to subscribers every other month (six times a year) sound advice, authoritative guidance, methods of diagnosis and treatment which these clinicians themselves are using and which you can use—*will use!*—in your own practice.

Turn to Page 3 for further details of the January Number.

SAUNDERS ADVERTISEMENT Continued on PAGES 3, 4, 5

SUBJECT INDEX TO THIS ISSUE

The letters used to explain in which department the matter indexed appears are as follows: The Star (*) indicates an Original Article; "ab," abstract; "E," Editorial; "C," Correspondence; "Ml," Medicolegal; "ME," Medical Economics.

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WATER BALANCE IN SURGERY

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AND
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ANN ARBOR, MICH.

The importance of water to the human organism is greater than that of any other substance. It normally comprises 65 per cent of the total body weight and is fundamentally concerned with every physiologic process. For centuries the intake and output of fluids have been investigated by man, the observations of Sanctorius,[1] published in 1614, on the perspiratio insensibilis of water from the skin and lungs being classics of early scientific endeavor.

Rowntree [2] and, more recently, Underhill [3] have presented reviews of the literature on water metabolism. Basic studies on an accurate measurement of the water balance of human beings have been carried out by Newburgh and his associates [4] and we acknowledge the inspiration and counsel given by this investigator.

From the surgical aspect, water balance becomes most important in dealing with the patient who, because of his disease or treatment, cannot take in sufficient fluids by mouth to care for his needs. Water must then be supplied by the physician, and, while experience has been a fairly reliable teacher as to the amount of fluid to give, it was apparent to us that the handling of the water requirements of the sick patient by figures based on facts would be of merit.

Accordingly, during the past four years a series of investigations on the water exchange of surgical patients under the various conditions of disease and treatment has been carried out. Before presenting the significant results of these studies, a brief review of normal water exchange is in order.

NORMAL WATER EXCHANGE

Under conditions of health a nice adjustment between available and excreted water results in the maintenance of the water content of the body at a fairly constant level. The components of this water exchange can be listed in table 1.

Fluids drunk vary from about 800 to 2,000 cc. daily, the higher intakes usually occurring in hot weather when the vaporization loss is great. Water becomes available from food whether it is that of the diet or body material burned for energy. Food eaten generally furnishes more water than is commonly thought. In the first place, its water content will average close to 70 per cent of its total weight and, in addition to this, water is formed when the constituent proteins, fats and carbohydrates are oxidized for energy. From the two sources, each gram of solid food eaten furnishes approximately 0.9 Gm. of water, the total thus available from a routine maintenance diet amounting to from 1,000 to 1,500 Gm. daily. Even in starvation up to 500 Gm. of water daily becomes available from body materials used for energy.

On the excretory side, water lost in feces is generally insignificant compared to the loss through other channels. Body economy is shown here by the fact that although from 7 to 10 liters of fluid is poured into the upper half of the gastro-intestinal tract daily by various glandular mechanisms,[2] most of the water is absorbed in the lower part of the bowel and less than 150 cc. is lost with the stool.

Important water excretions are concerned with two physiologic processes; namely, the output of waste materials in solution through the kidneys, and the dissipation of body heat by the vaporization of water from the lungs and skin. The vaporizing process plays an important part in the control of body temperature and is a continuous process in that there is always some moisture in the breath and also on the surface of the body, even without activity by the sweat glands. Ordinarily a person likes to keep himself comfortably cool and avoid sweating. Under such circumstances Newburgh and his associates have established the constancy of approximately 25 per cent of body heat being dissipated by water vaporized, and from a determination of the exact amount of water so used have been able to calculate the daily caloric expenditure of individuals under routine activities.[4b] At the 25 per cent rate a group of their subjects was found to disperse from 1,000 to 1,500 Gm. of water daily. The remaining 75 per cent of body heat is dissipated by radiation, conduction and convection from the body surface. These later processes become much less effective as the environmental temperature increases and greater percentages of heat are then dispersed by vaporization, the sweat glands pouring water on the surface of the body for this purpose. Vaporization can well be regarded as the safety factor in heat dissipation, since without its action many of the higher environmental temperatures would be intolerable.

It is important to point out that the vaporizing process, in contrast to water for kidney function, is

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From the Department of Surgery of the University of Michigan Medical School.

Read before the Section on Urology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 13, 1936.

1. Sanctorius, S.: De statica medicina aphorismorum sectionibus septem comprehensa, Leipzig, Shürer, 1614, 200 1.

2. Rowntree, L. G.: The Water Balance of the Body, Physiol. Rev. **2**: 116 (Jan.) 1922.

3. Underhill, F. P.: Certain Aspects of Water Metabolism, Yale J. Biol. & Med. **4**: 579 (March) 1932.

4. (*a*) Wiley, F. H., and Newburgh, L. H.: An Improved Method for the Determination of Water Balance, J. Clin. Investigation **10**: 723 (Oct.) 1931. (*b*) Newburgh, L. H.; Wiley, F. H., and Lashmet, F. H.: A Method for the Determination of Heat Production Over Long Periods of Time, ibid. **10**: 703 (Oct.) 1931.

little affected by the amount of water available. There is no mechanism whereby, when the water supply is low, temperature can be kept within normal limits with the use of less water than usual. The vaporizing process may be regarded as having "preferential rights" on available water over that of the kidneys. In deprivation of water for long periods of time the urine output may drop to almost nothing, the skin becomes hot and dry, and insufficient water may be used to keep internal body temperature within normal limits; but water still continues to be vaporized from the skin and lungs, with dehydration increasing until death occurs.

On the other hand, the kidneys are markedly affected by the amount of water available and excrete the waste materials presented to them with the water left after the other processes have been cared for. Thus one finds large daily urine volumes of low specific gravity and small daily volumes of high specific gravity. With a good supply of available water from fluids drunk and food eaten the balance between the intake and the output of fluids is largely maintained by the kidneys using the surplus water. On this basis a good fluid intake is shown by a good urine output and a small urine volume of high specific gravity practically always means insufficient water.

With regard to the surgical patients, the data and conclusions from the study of this group can be presented from the fairly definite points of view of dehydration attendant on surgical operations, the daily water losses of surgical patients, the water balance of the dehydrated patient, and parenteral fluids.

DEHYDRATION ATTENDANT ON SURGICAL OPERATIONS

It is common knowledge that on the day of a major operation a low intake of fluids and food by most surgical patients decreases their supply of available water. The exchange for that day is further interfered with by the frequent occurrence of abnormal fluid losses. The purpose of our first investigation [5] was to determine these losses quantitatively when they seemed to be greatest; that is, in the warm operating room and the immediate postoperative recovery period of four hours, when the patient is bundled up in extra blankets and frequently perspires profusely.

TABLE 1.—*Components of Water Exchange*

Available Water	Excreted Water
1. Fluids drunk	1. Water of urine
2. Food: diet or body material	2. Water of stool
A. Water content	3. Water vaporized
B. Water of oxidation	

A group of eighteen patients undergoing a variety of general surgical operations was studied. The loss of fluid in the operating room by vomiting was insignificant. The blood loss was usually much greater than the amount estimated by the operating surgeon, a few of the volumes obtained being given in table 2. In general, the blood losses were greater when large areas were exposed and there was more or less continuous oozing of blood than with hemorrhage from spurting vessels.

The greatest fluid output during the operative and four hour postoperative period was generally the vaporization loss. This made up 700 cc. of the average of 1,000 cc. lost by blood, vomitus, urine and vaporization during this time. It was learned that this sweat loss could be appreciably reduced if the extra blankets of the old fashioned postoperative "ether bed" were done away with and the patient was simply transferred from the operating table to a bed with only the usual amount of covers but warmed with hot water bottles. Water needlessly excreted was thus saved and the urine output showed a corresponding increase in amount. The reduced covers have been adopted as a routine in our postoperative surgical care. Patients are no longer found weighed down with a mass of covers and sweating as if in a Turkish bath. There has been no increase in postoperative pulmonary complications with the new arrangement, and the patients are infinitely more comfortable.

TABLE 2.—*Volumes of Blood Loss*

Partial gastric resection	274 cc.
Excision of thyroglossal cyst	174
Repair of inguinal hernia	147
Repair of inguinal hernia	54
Hemorrhoidectomy	8
Appendectomy	14
Excision of retroperitoneal teratoma	546
Right radical mastectomy	1,272
Subtotal thyroidectomy	142
Subtotal thyroidectomy	361
Repair of ventral hernia	306

As a result of the restriction in fluid and food intake and the increased fluid losses, most patients dehydrate to some extent on the day of their operation. The plan of many surgeons of giving some fluids parenterally on this day, particularly to patients undergoing long, serious operations, is well founded. For the general run of cases, however, the dehydration is not severe and with the improvement of the first and second postoperative days a greater ingestion of fluid returns the water exchange to normal. Occasionally nausea and vomiting interfere with the ingestion of water from the gastro-intestinal tract, or throughout the period of the disease or treatment rest of the gastro-intestinal tract is desired. Fluids must be given parenterally to these patients and the physician can provide the proper amount only if he knows what daily fluid losses must be cared for. Our second study of water exchange [6] was to furnish data in this regard.

THE DAILY WATER LOSSES OF SURGICAL PATIENTS

As in the healthy adult, the excretion of water by the surgical patient is mainly for two normal functions: the carrying away of waste materials through the kidneys, and the dissipation of body heat. The loss of water in the stools is generally insignificant in surgical conditions and can be disregarded. Since the vaporizing process seems to have first claim on the available water and the kidneys function largely with what is left, our first problem was to learn what the vaporizing loss amounted to in a group of representative patients. Briefly, the method for this determination was as follows: The patient, transferred from his bed to a Bradford frame, was picked up and weighed at 8 a. m. The weight of all ingesta and excreta up to 8 a. m. the following morning was obtained, at which time the

5. Coller, F. A., and Maddock, W. G.: Dehydration Attendant on Surgical Operations, J. A. M. A. **99**: 875 (Sept. 10) 1932.

6. Coller, F. A., and Maddock, W. G.: The Water Requirements of Surgical Patients, Ann. Surg. **98**: 952 (Nov.) 1933.

patient was again weighed. The total insensible loss of weight for the twenty-four hour period was calculated by the following equation: Beginning weight — (end weight — ingesta + excreta).[4b] This total insensible loss is the result of the continuous vaporization of water from the skin and lungs and the respiratory exchange of carbon dioxide for oxygen. Water usually comprises more than 90 per cent of the insensible loss, so that for our purposes the consideration of the latter as entirely water loss occasioned little error.

Adult surgical patients convalescing smoothly from major operations were found to vaporize from 1,000 to 1,500 cc. of water daily. Two children weighing about 60 pounds (27 Kg.) each vaporized 850 cc. daily under similar conditions. This is the same amount that these individuals would vaporize when up and about at normal routine activities without sweating.

Several conditions encountered in surgery increase the insensible loss of water. A warm, moist skin is a common clinical observation in patients with hyperthyroidism. Several individuals with this disease were found to vaporize from 1,500 to 2,000 cc. daily.[7] This increase over the normal of from 1,000 to 1,500 cc. was not found to result from any abnormal process of heat dissipation associated with hyperthyroidism but was simply due to the fact that, with more heat to dissipate, more water was used for this purpose.

Fever is a common complication among sick surgical patients and is one in which, because of the increased heat production and active sweating, the vaporization loss would be expected to be increased. Such was found to be the case in the study of several patients with infections. Water vaporized varied from 1,500 to 2,500 cc. daily. In general, for the sick surgical patient water for vaporization can be safely estimated at 2 liters a day.

With this figure for vaporization at hand, water for urine is the next problem. The amount available should be sufficient to permit the kidneys to excrete the waste materials presented to them without having to work at their maximum capacity. For the sick surgical patient we believe this to mean an output of at least 1,500 cc. of urine daily.

TABLE 3.—*Minimum Amount of Water Needed to Excrete 35 Grams of Waste Material*

Kidneys	Maximum Concentrating Ability, Specific Gravity	Minimum Amount of Water Required to Excrete 35 Gm. of Waste Materials, Cc.
Normal	1.032-1.029	473
Diseased	1.028-1.025	595
	1.024-1.020	605
	1.019-1.015	850
	1.014-1.010	1,439

This volume was selected purely on a consideration of kidney function. Lashmet and Newburgh[8] determined the excretory capacity of normal and abnormal kidneys under conditions forcing them to work at their maximum concentrating ability. Figures on the minimum amount of water needed to excrete 35 Gm. of waste materials, a fair daily amount, were calculated from their data and are given in table 3.

From these figures it is evident that an individual with normal kidneys needs to excrete about 500 cc. of urine a day for normal function. With a twenty-four hour urine output appreciably less than this, retention of waste materials can be looked for, and the blood nonprotein nitrogen will generally be found elevated. With diseased kidneys, more than 500 cc. of urine daily is needed, the required volume increasing as the concentrating ability decreases. In instances of the most severe renal damage, in which the kidneys can concentrate urine to a specific gravity of only 1.014 to 1.010, the figures show that close to 1,500 cc. of water is required. A minimum output, then, of 1,500 cc. of urine daily will take care of the excretion of waste materials by kidneys of all ranges of function, and this is the amount allowed for urine in our estimations of water requirements. Larger urine volumes, particularly in instances of infections of the urinary tract, are often desirable.

TABLE 4.—*Water Needed for Excretions*

1. Water for vaporization	2,000 cc.
2. Water for urine	1,500 cc.
3. Abnormal losses of water—vomitus, and so on	.....
Total	3,500 cc.

Frequently abnormal losses of fluid have to be considered in the water exchange of the sick surgical patient. Blood, vomitus, drainage from intestinal and biliary fistulas, diarrhea, massive exudation from inflamed surfaces, and sometimes sputum may remove important amounts of water and materials from the body. Such losses are "absolute losses" in that they carry out no physiologic function and take water that is needed for normal processes. The amount of these abnormal losses, by actual measurement or estimation, should be recorded on the patient's record by the nursing staff, so that they can be included in the calculations of water requirements.

When a patient is taking nothing by mouth, the only water available daily to care for the excretions, without producing dehydration, is that coming from body glycogen, fat and protein burned for energy. This source seldom furnishes more than 500 cc. daily, and the amount can well be forgotten in the calculations of water to be given to the sick patient, thus having a little extra supply. The excretions are the factors to care for in maintaining body fluids, and these can be summarized as in table 4.

If the patient is taking some fluid by mouth, that amount can be deducted from the 3,500 cc. total. If abnormal losses are occurring, they should be added, since with a failure to do so the seemingly sufficient 3,500 cc. total may be entirely inadequate. The surgeon who is quick to recognize the signs of dehydration in a patient seen for the first time may overlook the same signs when they occur in a patient he is seeing every day and who is receiving apparently a good supply of water but is actually dehydrating because of abnormal fluid losses. The resulting poor output of urine is often erroneously attributed to a reflex or toxic suppression of kidney function, whereas the real fact is that the patient has not been given sufficient water. This point cannot be too strongly emphasized.[9] There are many causes of anuria, but no others should be considered until the water exchange of the few previous days has been checked over and dehydration as the etiologic factor has been eliminated.

7. Coller, F. A., and Maddock, W. G.: Water Balance in Patients with Hyperthyroidism, West. J. Surg. **41**: 438 (Aug.) 1933.

8. Lashmet, F. H., and Newburgh, L. H.: A Comparative Study of the Excretion of Water and Solids by Normal and Abnormal Kidneys, J. Clin. Investigation **11**: 1003 (Sept.) 1932.

9. Cabot, Hugh, and Iber, F. C.: Anuria, Proc. Staff Meet., Mayo Clin. **8**: 354 (June 7) 1933.

WATER BALANCE OF THE DEHYDRATED PATIENT

Patients who enter the hospital in a dehydrated condition present an additional problem in water balance.[10] An amount of water sufficient to maintain body fluids is not enough for them, but an additional amount is necessary to restore the body water previously lost. If one knew how much fluid had been previously lost, water for its restoration could be given in a quantitative fashion similar to water for the maintenance of body fluids. There are no quantitative tests to show the degree of dehydration, so the only answer to the problem seemed to be a determination of the amount of water individuals need to lose in order to show the common clinical signs of dehydration, and then to provide that amount of additional water when patients are seen with those signs.

TABLE 5.—*Amounts Equaling 6 per Cent of Various Body Weights*

Body Weight	6 per Cent
10 Kg., or 22 lbs.	600 cc.
20 Kg., or 44 lbs.	1,200 cc.
60 Kg., or 132 lbs.	3,600 cc.
80 Kg., or 176 lbs.	4,800 cc.

To furnish data in this regard, two normal subjects were fed a dry maintenance diet for a number of days, during which time they were dehydrated by the withholding of water until the beginning signs of serious dehydration appeared; that is, a dry hot skin, a dry tongue, sunken eyes, a little fever, and a urine output insufficient to excrete the normal waste materials. The last mentioned was the only readily measurable sign and was used in such a way that the dehydration of both subjects was continued until their blood nonprotein nitrogen had increased to a little above 40 mg. per hundred cubic centimeters. When this occurred, all the common clinical signs of dehydration mentioned were well established. As evidence of the adverse conditions under which the kidneys were working the urine of the 26 year old subject finally reached a specific gravity of 1.041 and contained a trace of protein and more than the usual number of casts and erythrocytes.

The water balance data of both subjects showed that the signs of serious dehydration produced were the result of being depleted of an amount of water equal to approximately 6 per cent of their body weight. Observations by several members of the investigating staff during the past four years support the opinion that, when the signs of serious dehydration are present in a patient, body fluids of an amount equal to at least 6 per cent of the patient's body weight have been lost. The figures in table 5 show what this amounts to for individuals of various weights.

While we know that these volumes of fluid are called on in emergencies, it is not practical to regard them as a true reserve of fluid, since beyond the first few hundred cubic centimeters they are given up with increasing reluctance and to the detriment of the whole organism. For children the relatively small amount of fluid that represents 6 per cent of the body weight probably accounts for the rapidity with which, under adverse conditions, they become sick and dehydrated.

When water was again given to our experimental subjects the urine volume did not immediately increase but nearly all the first day's water intake was retained to replace the body fluid previously lost. It was perfectly apparent that the major need for water was to restore to normal some of the internal chemistry that had been upset during the dehydration period. Water to relieve dehydration and water for vaporization was decidedly more important than water for kidney function, and it was only when the former had been cared for that sufficient water became available for urine.

In considering the water requirements of a 60 Kg. patient who enters the hospital with the beginning signs of serious dehydration well established, a calculation of the amount of fluid to give during the first twenty-four hours should include the factors given in table 6. This is a lot of fluid, but studies by us on several dehydrated patients have shown that such quantities are necessary to provide for the dehydration, for vaporization and abnormal loss, and then to have enough water left for kidney function. Of course, once the depleted fluids have been taken care of, much less water is needed to maintain normal fluid exchange. Besides seeing to it that sufficient fluids are provided, a quantitative consideration of the water requirements of the sick surgical patient will also avoid the administration of too much fluid.

PARENTERAL FLUIDS

So far, the quantity of fluid to be given parenterally in order to maintain body fluids or treat dehydration has been considered. The kind of fluid to give also merits some thought.

The fundamental proposition back of the choice of fluid is that of supplying as nearly as possible what the patient needs. There is no question that some dextrose should be given to all patients requiring water parenterally. It is an ideal fuel for energy, it prevents or relieves ketosis, and it protects the liver. In contrast to dextrose, the indications for the administration of sodium chloride are not quite so simple.

TABLE 6.—*Water Requirements in Dehydration in a Dehydrated Patient Weighing 60 Kg.*

1. Water for vaporization	2,000 cc.
2. Water for urine	1,500 cc.
3. Abnormal loss, if any, during the 24 hours	.....
4. Water to restore depleted fluids, 6 per cent of 60 Kg.	3,600 cc.
Total	7,100 cc.

The excellent observations of Hartwell and Hoguet,[11] Orr and Haden,[12] McIver and Gamble[13] and Hartman and Elman[14] have firmly established the value of saline solutions in replacing the sodium chloride depletion associated with the loss of secretions from the gastrointestinal tract. A distinct tendency exists, however, for the routine use of saline solutions for all parenteral administrations of fluid, without regard to whether sodium chloride is needed or not. Matas[15] in 1924 pointed out the serious drawbacks of such a plan, emphasizing in particular the occurrence of degenera-

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11. Hartwell, J. A., and Hoguet, J. P.: Experimental Intestinal Obstruction in Dogs, with Special Reference to Cause of Death and Treatment by Large Amounts of Normal Saline Solution, J. A. M. A. **59**: 82 (July 13) 1912.

12. Orr, T. G., and Haden, R. L.: Chemical Factors in Toxemia of Intestinal Obstruction, J. A. M. A. **91**: 1529 (Nov. 17) 1928.

13. McIver, M. A., and Gamble, J. L.: Body Fluid Changes Due to Upper Intestinal Obstruction, J. A. M. A. **91**: 1589 (Nov. 24) 1928.

14. Hartman, A. F., and Elman, R.: The Effects of Loss of Gastric and Pancreatic Secretions and the Methods for Restoration of Normal Conditions in the Body, J. Exper. Med. **50**: 387 (Sept.) 1929.

15. Matas, Rudolph: The Continued Intravenous Drip, Ann. Surg. **79**: 643 (May) 1924.

tive changes in heart muscle and kidneys, and edema of the lungs. Edema is not uncommonly seen among surgical patients receiving fluids parenterally. Jones and Eaton [16] presented a review of thirty-four such cases and emphasized the predisposing factor of undernutrition as shown by low total serum proteins and serum albumin. Other factors, such as the excessive administration of water and salt, profuse surgical drainage and the general effects of sepsis, were also pointed out. These factors are commonly present in seriously ill patients, and it is often to just these individuals that the parenteral administration of fluids is so necessary and valuable.

From clinical observations it had been our impression that, while many conditions predisposed to the retention of water in sick surgical patients, the precipitating factor was frequently the indiscriminate use of saline solutions. Largely to corroborate this opinion, a study was made of the water exchange of three groups of such patients,[17] each receiving approximately 3,500 cc. of one of the commonly used intravenous fluids daily for several days as a part of their necessary postoperative care.

The first group was given 5 per cent dextrose in physiologic solution of sodium chloride. All of them retained water and gained weight, one developing edema of the lower part of the back and of the ankles. When the intravenous solution was changed to 5 per cent dextrose in distilled water the retained water was promptly given up. This finding is worthy of special emphasis. It was not necessary to limit the administration of water to these patients or to use diuretics to get rid of the edema fluid; the stopping of the sodium chloride was all that was necessary.

The importance of poor general condition to water retention was brought out by the fact that five patients convalescing nicely from the treatment of surgical lesions and whose general condition was excellent did not retain water when given 5 per cent dextrose in physiologic solution of sodium chloride for several days. One of them had previously retained water when given this solution at the time of having a moderately severe systemic reaction from an acute pyogenic infection about the elbow.

The second group of seven sick patients was given 5 per cent dextrose in Ringer's solution. Six of the seven retained water, but it was our impression that the amount retained was a little less than that of the group receiving 5 per cent dextrose in physiologic solution of sodium chloride. This apparent advantage of Ringer's solution over physiologic solution of sodium chloride may be due to the small amount of potassium chloride and calcium chloride present in the former. Ringer's solution is now our fluid of choice for patients needing sodium chloride.

The third group of sick patients received 5 per cent dextrose in distilled water. None of them retained water, their exchange being approximately the same as if the solution had been given by mouth. As was expected from clinical observations, with no abnormal loss of sodium chloride the plasma carbon dioxide combining power and chlorides of these patients did not change materially when given the dextrose in water for six days. One has no need to worry about washing salt out of the body with such treatment.

Considering that twelve out of the thirteen sick patients receiving 5 per cent dextrose in saline solutions retained water, it is apparent that warnings concerning the development of edema with the indiscriminate use of sodium chloride solutions are well founded. We believe that the only reason why edema is not more frequently seen with such treatment is that the solutions are generally given for only a day or two. While edema developed in only one of the patients studied, in several of them it was well on the way to do so and would have if the solutions had been given for a few days longer. Waterlogged tissues are often seen in surgical patients coming to autopsy. Undoubtedly an excess of salt solution is a contributing factor in some instances. The first question in the mind of the surgeon on finding edema in a patient who has been receiving fluids parenterally should be "How much salt solution has been given?"

It is difficult to lay down hard and fast rules to cover the proper administration of saline solutions to all patients. Recently the reasons for the giving of parenteral fluids to 100 general surgical patients at the University Hospital were analyzed.

Twenty per cent of them had been vomiting and needed some sodium chloride besides water and dextrose. Ringer's solution was given here, but not too much of it. To avoid the administration of excessive amounts of salt, two procedures can be followed: Patients with a considerable loss of gastro-intestinal secretion, particularly those in whom the loss has occurred before admission to the hospital, so that consequently little is known about it, should have a blood chloride and a carbon dioxide combining power study done to show the depletion of chloride and basic ions respectively. If these are found to be low, from 1,500 to 2,000 cc. of Ringer's solution can be given daily. The blood chemistry studies should be repeated every two days while the salt solution is being given, so that it can be stopped when these electrolytes are up to normal. Since the loss of one of these electrolytes is usually greater than the other and the replacement of one is therefore needed more than the other, chlorides in alkalosis and sodium in inorganic acidosis, it is desirable to alternate the saline solution liter for liter with 5 per cent dextrose in water during the correction period. This provides an immediate excess of water, and with this the kidneys can generally be relied on to excrete the less needed electrolyte. Alkalosis and acidosis can thus be taken care of with the same solutions.

The second plan is applicable when the patient is in the hospital and the loss of gastro-intestinal secretion, as by vomiting, has been measured. It is satisfactory then to give parenterally an amount of Ringer's solution equal to the amount of vomitus. The concentration of sodium chloride in this solution (or in physiologic solution of sodium chloride) is always greater than that in vomitus or other secretions of the gastro-intestinal tract.[18] With such a procedure the electrolyte loss is well taken care of, and the mistake of giving close to 30 Gm. of sodium chloride, the amount present in 3,500 cc. of physiologic solution of sodium chloride or Ringer's solution, to cover the 5 Gm. loss of sodium chloride in a liter of vomitus, is avoided.

That sodium chloride is not needed as a routine was shown by the fact that 80 per cent of the patients

16. Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema, Arch. Surg. **27**: 159 (July) 1933.

17. Coller, F. A.; Dick, V. S., and Maddock, W. G.: The Maintenance of Normal Water Exchange with Intravenous Fluids, J. A. M. A. **107**: 1522 (Nov. 7) 1936.

18. Dick, U. S.; Coller, F. A., and Maddock, W. G.: Data to be published.

analyzed were given fluids parenterally simply because through their disease or treatment they were unable to take sufficient fluids by mouth to maintain a normal balance. These patients had not been vomiting and were not dehydrated. What they needed was sufficient water daily to provide for their normal excretions, and enough dextrose to prevent ketosis. Throughout the study of the sick patients receiving fluids intravenously the suitability of 5 per cent dextrose in distilled water for furnishing enough dextrose and maintaining a normal water exchange was apparent.

Concerning the mechanics of giving fluids parenterally, the intravenous route has been preferable in our hands to subcutaneous infusions. The main apparatus consists of a 700 cc. containing bottle, a drip tube, and pure gum rubber tubing throughout. Intravenous cannulas have seldom been employed, it being our experience that phlebitis was more common with them than with ordinary intravenous needles, the site of which is changed daily. The rate of flow is never faster than 500 cc. an hour. This permits the administration of a good volume of fluid in a few hours during the daytime, if possible, so that the night is left undisturbed for rest and sleep. At the same time, with this rate there is no possibility of overloading the heart. No particular effort is made to keep the intravenous fluid at a constant temperature during its administration, since this factor is apparently unimportant when the fluid is given slowly.

COMMENT

There are many questions on water balance and parenteral fluids in relation to surgical patients that have not been answered in this paper. The problems studied have been interesting and the data obtained have had gratifying clinical applications. The whole subject forms an important chapter in preoperative and postoperative care, and its skilful handling often saves the life of the seriously ill patient.

University Hospital.

ABSTRACT OF DISCUSSION

DR. LEONARD G. ROWNTREE, Philadelphia: Everything that the authors have said constitutes sane and safe advice in relation to the handling of the surgical patient from the standpoint of water. Two thirds of the human body is composed of water, and consequently the water balance is of tremendous significance to the proper functioning of the organism under all conditions. During and after surgical intervention there is often a tremendous strain on the organism, and the importance of water is greatly enhanced. Urologists work mostly with the kidney and the urinary system, which is concerned with the excretion of water and water soluble substances that are carried off as waste material. I have always been interested in the urologic point of view in relation to excretion by the body. I have often wished that I could go back twenty years, or preferably thirty, and grasp at an earlier date the possibilities that urology has to offer relative to failure of excretion and the development of disease. The kidney is responsible to a large extent for what Cannon has termed hemeostasis; that is, keeping the blood constant in volume and composition, a condition essential to optimum efficiency. In this connection one has to consider not only the side of hemeostasis in keeping the blood pure but that which has been emphasized this afternoon and was formerly emphasized by Claude Bernard, "the volume obligatoire"; that is, a sufficient quantity of urine for the complete solution of the waste products of metabolism. What happens at the time of operation? Water is withheld before and after operation. This is necessary from the standpoint of the intestinal tract, but water should not be withheld from the body as a whole. The night before an operation, the patient is usually given a dose of some purgative, frequently castor oil. The figures that the authors have given appear rational: 3.5 liters a day for a patient who is not dehydrated and 7 liters a day for the patient who is dehydrated and in whom the depots of water in the body have been exhausted. These figures can serve only as guides and not as fixed rules. I believe it would be a mistake to restrict fluids to 5 per cent dextrose. There are many instances in which other substances, particularly electrolytes, are essential. These should be supplied to meet the individual needs. One can overdo this water business and produce water intoxication. Attempts have been made to devise a test whereby one can tell whether or not the water need is great in an individual. The disappearance of McClure's saline "bleb" has been suggested.

DR. A. J. SCHOLL, Los Angeles: Maddock and Coller's paper and Dr. Rowntree's discussion, with their previous papers, have covered almost all there is to say about water balance. For years physiologic solution of sodium chloride has been used almost universally following operations, 3,000 and 4,000 and sometimes 5,000 cc. a day. The authors stated that in twelve out of thirteen of their cases a retention developed when saline solution was given daily for more than three or four days. Keith has recently shown that it is not the chloride but the sodium radical that causes the retention. If the sodium is changed to potassium, retention does not occur; there may be a diuresis. Keith states that as yet he is not ready to recommend the use of the potassium salt, but patients such as the authors discussed do not need the potassium any more than they need the sodium or chloride; what they need is simply more fluids. Of course, in an occasional case, after vomiting or after excessive sweating, there is a loss of body chlorides and it must be replaced. Thirty years ago the farmers in California found that if they drank salted oatmeal water they were less liable to have heat exhaustion and that they were better able to go through the heat of the day. They did not know what the oatmeal water did, but it kept them from becoming exhausted in the heat. During the building of Boulder Dam the heat at the base of the canyon was terriffic. There were days when the thermometer registered from 110 to 115 F. in the base of the river bed. The men drank prodigious amounts of water; 10, 15 or 18 liters a day was common. They came out of the canyon cooled off, and the salt from their sweat crystallized on their faces and on their arms like frost on a window. Heat exhaustion was common until it was suggested that salt be added to the drinking water; after that the men could get only salt water to drink. This addition of salt to their water practically stopped the occurrence of heat exhaustion.

DR. WALTER G. MADDOCK, Ann Arbor, Mich.: I thank Dr. Rowntree and Dr. Scholl for emphasizing the important points in their discussion. The administration of too much water occasionally occurs. While a thoughtful consideration of water exchange is largely important in seeing to it that the patient receives sufficient water, it also serves to prevent the giving of too much fluid. My plea is for not too much fluid or too little fluid, but the correct amount, and it can be calculated. As has been stated, the question of whether to furnish sodium chloride along with water and dextrose to patients requiring parenteral fluids must be decided on a consideration of the needs of each individual patient. A routine procedure will fail to take care of the important exceptional case. In my hands the administration of parenteral fluids with due regard to both the amount and the kind of fluid to give has yielded gratifying results.

Croup in Childhood.—Croup, however, is not a disease but a symptom, and the practitioner must determine the underlying pathology. The conditions which give rise to croups are congenital laryngeal stridor; laryngismus stridulus; laryngitis stridulosa; acute laryngitis, diphtheritic laryngitis; retropharyngeal abscess; papilloma of the larynx, or upper trachea. Not all of these conditions have a surgical bearing so far as treatment is concerned, but each of them must be considered in making a diagnosis.—Crooks, James: Surgical Aspects of Croup in Childhood, *Practitioner* **137**:709 (Nov.) 1936.

THE PATHOLOGIC CHANGES RESULTING FROM VITAMIN DEFICIENCY

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Descriptive accounts of the pathologic changes resulting from each vitamin deficiency would make a voluminous report, dry and nonstimulative. The subject will be presented with the attitude that each deficiency causes distinctive functional disturbances and is accompanied by distinctive morphologic changes which together may reasonably be regarded as primary effects. In consequence, it is assumed that some of the general disturbances in nutrition, blood formation and growth, common to several of the vitamin deficiencies, are in all probability secondary nonspecific effects. The primary morphologic effects, as far as known, when analyzed all prove to be manifestations of retardation or suppression of normal processes. In recovery from a vitamin deficiency following restoration of the vitamin to the diet, normal morphologic sequences are resumed and proceed for a brief period at a rate exceeding the normal, until repair is completed. Possibly physiologic activities of certain types may be suppressed without demonstrable tissue or cytologic effects occurring. In the search for initial specific morphologic changes the pathologist has opportunity to make his humble contributions to the goal common to all biologic sciences—the understanding of the chemistry of living cells.

The pathologic or morphologic characterization of a vitamin deficiency involves a dual basis: (*a*) the changes in consequence of the deficiency, and (*b*) the changes accompanying recovery from the deficiency ending in restoration to normal structure.

VITAMIN A DEFICIENCY

Specific Pathology.—The primary effect of vitamin A deficiency is on epithelial structures. The sequences are atrophy of the epithelium concerned and the substitution for it of a stratified keratinizing epithelium, identical in appearance in all locations, and arising from focal proliferation of basal cells. These sequences have been carefully worked out in rats [1] and guinea-pigs.[2] Since replacement by keratinizing epithelium in many organs has also been found in human infants,[3] in the monkey (Macacus rhesus)[4] and in the albino mouse,[5] and since gross changes indicate the same histologic changes in swine,[6] in dogs,[7] in rabbits,[8] in cattle,[9] and in the domestic fowl,[10] the conclusion seems unavoidable that vitamin A is essential in most vertebrate species and that its withdrawal is followed by a common effect on epithelial structures. For convenience this change will be called keratinizing metaplasia, regardless of exact connotations of the term. The detailed studies by Howe and myself [11] have led us to the conclusion that the absence of vitamin A creates a starvation specific for many epitheliums. The consequence is atrophy, which progresses to a state wherein the cells, although having the appearances of viability, become inert in physiologic activities and in their rôle of covering membranes. An invariable sequence in pathology is that a break in the continuity of a tissue is followed by reparative proliferation. In vitamin A deficiency the basal cells normally concerned in maintaining the integrity of epithelium respond by active mitotic division. As the basal cells have a focal distribution in all nonstratified epitheliums, the next effect of the deficiency after atrophy is the appearance of scattered areas of proliferative activity beneath the original epithelium. The new (reparative) cells by their continued growth undermine and replace the original epithelium and, regardless of previous function and morphology of the region, develop into a stratified keratinizing epithelium. An important feature in explanation of much of the gross pathologic change is the fact that this replacement epithelium is identical in all locations and comparable in all its layers with epidermis. It has a continuous layer of basal cells—a stratum germinativum—in continuous proliferative activity while superficially it is continuously casting off keratinized cells. The striking gross pathologic condition of vitamin A deficiency in animals and in human infants is the outcome of the accumulation of keratinized epithelial cells in many glands and their ducts and in other organs. In glandular organs, cysts of considerable size are formed, filled with yellowish cheesy masses of keratinized cells. In the lungs of human beings as well as of experimental animals this process leads to cyst formation, bronchial occlusion, and consequences such as bronchiectasis and atelectasis. Early students of vitamin A deficiency, chemists and physiologists, neglected to study these cysts and believed them to be abscesses. Hence, for many years vitamin A was believed to protect against infection. As a matter of fact, the plugs of desquamated epithelial cells in ducts, bronchi and trachea, opening as they do on regions normally infected with bacteria, provide a culture medium for their growth. In spite of the fact that in both human beings and laboratory animals such bacterial growths were frequently found by us, very rarely was there invasion of the tissues, presumably because of the protection afforded by the stratified epithelium.

Distribution of the Keratinizing Metaplasia.—In the rat, the order of response to vitamin A deficiency by metaplasia is:

1. Salivary glands, including submaxillary, parotid and all accessory glands of the tongue, buccal cavity and pharynx.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the author's reprints.

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2. Respiratory tract, including nares, maxillary sinuses, Jacobson's organ, trachea and bronchi.

3. Genito-urinary tract, including the renal pelves, ureters, bladder, epididymis, prostate, seminal vesicles, coagulating glands, uterus, oviducts and accessory sex glands of the vulva.

4. Eye and parocular glands, including the corneal and palpebral conjunctiva and the harderian, intra-orbital and extra-orbital lacrimal glands and the meibomian glands.

In the guinea-pig, lesions of the conjunctiva and parocular glands did not develop in our experiments even though advanced lesions (keratinizing metaplasia and its consequences) were found in all other locations as recorded for the rat. A marked difference in behavior as compared with the rat was early and extraordinary degrees of metaplasia in the uterus and bladder.

In human infants, keratinizing metaplasia has been found in the conjunctiva, mucosa of the nares, accessory sinuses, trachea, bronchi, pancreas, renal pelves, ureters, salivary glands, uterus, and periurethral glands. The commonest and earliest appearance of the metaplasia is in the trachea and bronchi. Next in frequency and sequence is the pelvis of the kidney. The early effect of the deficiency on the respiratory mucosa is a satisfactory explanation of the frequency, severity and persistence of the pneumonias that have been in most instances responsible for death in vitamin A deficient infants.

In the human being, as in the rat, involvement of the eye occurs late. The first change is metaplasia of the epithelium of the cornea and of the conjunctival sac. Atrophy and metaplasia of ducts of the parocular glands contribute to the consequences of the accumulation of keratinizing cells in the conjunctival sac. The cornea becomes vascularized, edematous and infiltrated with leukocytes. Infection of the cornea, favored by excessive accumulation of keratinized cells, may lead to ulceration of the cornea and hypopyon.

The Teeth in Vitamin A Deficiency.—The continuously growing incisor teeth of rodents—rats and guinea-pigs—are profoundly affected owing first to atrophy and metaplasia of the enamel forming organ and subsequently to atrophy and cessation of or irregular functioning of odontoblasts. Enamel formation is suppressed, and striking deformities of the dentin result.[12] May Mellanby[13] has summarized her work on teeth in an excellent review and presents convincing proof that absent or defective enamel and dentin formation are consequences of vitamin A deficiency.

Boyle[14] has described in the tooth germ of a human infant with vitamin A deficiency enamel organ changes comparable to those we have studied in rodent incisor teeth. In all probability, vitamin A deficiency, during the formative period of teeth, outranks all other vitamin deficiencies in importance.

Secondary Effects of Vitamin A Deficiency.—While the keratinizing metaplasia produces impressive gross lesions which are often the immediate cause of death, as in the lungs of infants and in experimental animals leading to complete suppression of urine by occlusion of ureters and renal pelves, it must be remembered that it is a late effect of the deficiency; in fact, the consequences of attempted repair following atrophy of essential epitheliums. The effects on the organisms as a whole which follow reduced activities of many epitheliums in earlier periods of atrophy preceding metaplasia replacement must be considered.

The secondary effects, common both to infants and to laboratory animals, are (1) loss of weight due largely to loss of fat in all storage depots, but also to atrophy of musculature and many organs which do not undergo keratinizing metaplasia, (2) anemia, (3) cessation of growth of bones, (4) degenerative lesions of skeletal muscle, and (5) lymphoid hypoplasia of the spleen.

The loss of fat in experimental animals in the absence of vitamin A takes place in spite of abundant fat in the diet, but this is also the case with other vitamin deficiencies accompanied by emaciation, notably the B_2 complex. The anemia in infants and experimental animals is accompanied by hemosiderosis in the spleen and liver and, finally, by atrophy of the spleen and bone marrow.

In animals, restoration of vitamin A to this diet is followed by regeneration of the bone marrow, disappearance of hemosiderin from the spleen and liver, and in the rat also in the spleen by an active hyperplasia of lymphoid tissue and an outburst of erythroblastic activity. Again, the anemia and hemosiderosis are not peculiar to vitamin A deficiency. Both occur in striking degree in animals in vitamin B_2 complex deficiency and in long continued partial vitamin C deficiency.

The cessation of growth of bone is due to cessation of proliferative activity of the epiphyseal cartilages. A narrow band of atrophic cartilage results, which becomes bounded by a thin plate of bone on the diaphyseal side. In recovery from vitamin A deficiency the cartilage regenerates, and blood vessels from the diaphyseal marrow penetrate the limiting bony plate, and normal endochondral bone formation is resumed. The effect on bone is that common to any athrepsia, of vitamin deficiency origin or otherwise.

The degeneration of skeletal muscle in vitamin A deficiency, while often very striking and even terminating in calcification, is also common to deficiencies of diverse causation.

Lesions of the nervous system, evidenced by degeneration of the myelin sheath, have been described by several workers, notably in swine, fowls and cows by Hughes and his associates,[15] in rats by Zimmerman[16] and Aberle.[17]

Recently, Edward Mellanby,[18] on the basis of studies of the trigeminal and a few other nerves by the capricious Marchi technic, suggests that the epithelial responses to vitamin A deficiency are secondary to lesions of afferent nerves.

Degeneration of the myelin sheath is common to so many disorders of man and animals as the result of several vitamin deficiencies and divers causes that very careful work will be required to establish a specific relationship of its presence to vitamin A deficiency.

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For the present it seems logical to regard the lesions of the nervous system as among the late secondary consequences of vitamin A deficiency.

Repair in Recovery from Vitamin A Deficiency.—The lesions of vitamin A deficiency, uncomplicated by destruction of tissue by infectious process, disappear rapidly after restoration of the diet. In rats, gain in weight, resumption of growth in bones and teeth, and regeneration of the bone marrow and spleen become apparent in from six to eight days. Reparative changes in the metaplastic epithelium begin as early as the fifth day. The initial changes are separation of superficial keratinized cells and vacuolization of cells of intermediate layers. The epithelium becomes divided into two zones by further vacuolar degeneration and leukocytic infiltrations. The superficial zone of cells degenerate, the deep zone, consisting of the lowermost layers of cells corresponding to the stratum germinativum of the epidermis, survives and the cells proceed to differentiate into the type of epithelium originally present. On the whole, the change back to the normal epithelium is an abrupt one and affords further evidence that the primary consequence of vitamin A deficiency is epithelial and not of nervous origin. This reparative sequence of the epithelium has its normal counterpart in changes in the vagina of rodents during that part of the estrous cycle in which the cornified vaginal mucosa returns to the mucous type.[19]

VITAMIN C DEFICIENCY

Of vitamin C deficiency, only the specific pathologic lesions will be considered. The pathology of scurvy is well known and covered in the books by Aschoff and Koch,[20] Hess [21] and others.

The requirements of all animals for vitamin C are not known. Scurvy, duplicating that in man, can regularly be produced in guinea-pigs and monkeys. The cow, rat, mouse, prairie dog, pigeon and domestic fowl do not require vitamin C in the diet; nevertheless it is found in their livers—evidence that these creatures can synthesize this vitamin.

The gross and microscopic pathologic changes of human scurvy, as seen in the infant and experimental scurvy in the guinea-pig, are so nearly identical that no reasonable doubt can be entertained with regard to applying to the human being the facts ascertained from the experimental studies.

In 1926 Wolbach and Howe [22] characterized the condition of scorbutus as the inability of the supporting tissues to produce and maintain intercellular substances. The effect is therefore on cells of mesenchymal origin in contrast to the ectodermal and entodermal effects of vitamin A deficiency. These conclusions were reached through histologic studies of human infantile scurvy and through studies of the histologic sequences, in growing guinea-pigs, of progressive scurvy and of the repair following administration of vitamin C in natural forms. Subsequently [23] further verification that vitamin C was the only missing factor in scorbutus concerned in the inability of tissues to produce intercellular material was obtained through the study of reparative processes following administration of crystalline cevitamic acid, orally and parenterally.

Further experimental proof of the correctness of this pathologic characterization was obtained [24] by a comparison of isolated fibroblasts during the organization of blood clots in the complete deficiency with those during the progress of recovery induced by the administration of vitamin C.

The intercellular substances concerned in vitamin C deficiency are the collagen of all fibrous tissue structures, the matrices of bone, dentin and cartilage, and all nonepithelial cement substance, including that of the vascular endothelium. The reparative proliferative powers of epithelial cells, endothelium, fibroblasts and osteoblasts are not impaired, while there is evidence of increased proliferation of osteoblasts, which in the periosteum and at the sites of endochondral bone formation undergo a striking change in morphology, taking on the appearance of young fibroblasts.

Aschoff and Koch [20] anticipated in part these conclusions from their studies of human material. They explained some features of the pathology of bone as due to failure of osteoblasts to form osteoid tissue and, by inference, the hemorrhage of scurvy as due to a failure of cement substance in blood vessels. Mechanical factors were emphasized as determining the sites of hemorrhages in bone, muscle, skin and alveolar processes of the jaws.

Soft tissue changes in vitamin C deficiency, human, and experimental in guinea-pigs, are hemorrhages in regions determined by mechanical stresses and trauma; also anasarca (human) and degenerations of skeletal and cardiac muscle. Hypertrophy of the heart occurs particularly in infants and children, attributed by Erdheim [25] to difficulties in respiration in consequence of the lesions of the ribs at the costochondral junctions. No such explanation can be applied to the cardiac hypertrophy of beriberi or B_1 deficiency. In long continued partial vitamin C deficiency in guinea-pigs, degeneration of skeletal muscle fibers becomes widespread. Affected fibers become completely necrotic. We have found this lesion common also in vitamin A and vitamin G (B_6 + lactoflavin) deficiency.

Goettsch and Pappenheimer [26] describe a diet with adequate vitamin content which leads to a progressive fatal degeneration of the voluntary muscles. The lesion of the individual fibers is identical with that of vitamin deficiencies A, G and C. Furthermore, it was shown by Pappenheimer and his associates [27] that the muscle degeneration was not associated with demonstrable changes in peripheral nerves or their motor terminals. Accordingly, the striking degeneration of muscles in long continued partial experimental scurvy [28] as in acute scurvy must be regarded as secondary effects of vitamin C deficiency. Anemia is another secondary effect of importance. In long continued partial vitamin C deficiency in guinea-pigs, large regions of bone marrow

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become devoid of blood forming cells and the seat of a deposit of homogeneous amyloid-like material.[28]

The important gross features of scurvy at all ages are hemorrhages and changes in the bones. The most striking lesions are the subperiosteal hemorrhages and those in the epidiaphyseal junctions of growing bones. All the pathologic features of scurvy are understandable only on the basis of the characterization as a condition of cessation of formation and maintenance of intercellular substances. Calcium metabolism is not primarily affected. In the first period of scurvy, existing cartilage trabeculae at epidiaphyseal junctions become more densely calcified than normally.[29]

In advanced scurvy, calcium salts are liberated through the resorption of bone matrix, which is the process of the osteoporosis of scurvy.

In general, the pathologic picture of scurvy is produced by the resorption of intercellular materials and by the absence of formation of intercellular materials in growth and reparative reactions. Hemorrhages are due to mechanical weakness, occasioned by the lack of collagenous material in fibrous tissue structures and in bone. Diminished cohesion of endothelial cells contributes to the ease with which moderate stresses occasion bleeding in skin and muscles. In the hemorrhages from the gums, the resorption of alveolar processes and the loosening of teeth, the two factors of stresses and loss of intercellular materials are apparent, the first affecting the second.

At the epidiaphyseal junctions in growing bones, the first demonstrable change in experimental scurvy is an increase in the number of osteoblasts applied to the cartilage columns. Formation of cartilage and bone matrices ceases, and the osteoblasts become elongated, assume the shapes of fibroblasts and migrate toward the diaphysis. Here these cells become surrounded by liquid, presumably a deficient product of continued activity toward matrix formation, and give rise to an apparent region of edematous connective tissue at the ends of the diaphysis, the gerüst mark (framework marrow) of German authors.

Marked changes in the epiphyseal cartilage occur because of resorption of matrix. Union between epiphysis and diaphysis becomes severed because the trabeculae of the spongy bone no longer communicate with epiphyseal cartilage, owing to the cessation of formation of periosteal bone. This disunion permits movement of the epiphysis in relation to the diaphysis, and traumatic fragmentation occurs, producing the trümmerfeld zone or zone of disorganization between gerüst mark and epidiaphyseal line. Hemorrhage complicates the picture. This accounts for the complete separation and dislocation of epiphyses so often seen in scorbutic infants and rarely at costochondral junctions in adults. Proliferation of cells, osteoblasts, of the periosteum in contact with the cortical bone is continued in growing bone and is a conspicuous histologic feature of scurvy in infants. A layer of cells without intercellular material thus results and separates periosteum from bone; hence the massive subperiosteal hemorrhages so characteristic of scurvy in infants. These sequences have been worked out in guinea-pigs, yet each stage has been seen in human material.

In growing teeth (incisors) of guinea-pigs, formation of dentin ceases and the pulp becomes separated from the dentin by liquid, which may be interpreted as due to the continued production by the odontoblasts of a liquid product. Presumably, teeth in process of formation in infants may be similarly affected in scurvy, but direct demonstration is lacking.

Repair of Scurvy.—Histologic repair following administration of vitamin C in natural foods or as cevitamic acid is dramatic in character and promptness, and in the small amounts of the remedy required. Newly formed dentin, collagen and bone matrix can be seen after twenty-four hours. Osteoblasts, disguised in morphology as fibroblasts, resume their rôle in formation of bone matrix. New capillary formation becomes possible, so that repair by granulation tissue formation proceeds in organization of blood clots and subsequent callous formation where the hemorrhages were in contact with bone. All normal processes of repair are resumed, infractions and fractures heal and subperiosteal hemorrhages become in part organized and ossified. In guinea-pigs, dentin formation is resumed in volume and rapidity suggestive of the jelling of a liquid material between pulp and old dentin.

VITAMIN D DEFICIENCY OR RICKETS

The physiologic rôle of vitamin D, whether or not identical with the pure substance calciferol or viosterol, in the metabolic processes concerned in the deposition of calcium phosphate in bone is not clear, particularly in relation to the experimental production and cure of rickets in white rats. In the absence of vitamin D, proper amounts and ratios of calcium and phosphate in the diet prevents rickets, yet vitamin D cures rickets produced in the rat by dietary methods. Likewise, restoration of a proper calcium and phosphate intake is curative.

Experimental rickets can be produced also in swine,[30] rabbits,[31] the monkey [32] and the domestic fowl.[33]

Important landmarks in the progress of knowledge of the pathology of rickets are the publications of Pommer,[34] Schmorl,[35] Erdheim [36] and Pappenheimer.[37] An adequate bibliography is contained in Hess's [38] book.

In white rats, experimental rickets, in all phenomena amenable to study, duplicates human rickets. This applies with particular force to the histologic sequences in the development of the lesions and in the repair.

The pathologic conditions of rickets arise from retardation and suppression of sequences primarily concerning cartilage in the endochondral formation of bone and from failure of bone matrix or osteoid to calcify in all locations.

Briefly stated, the sequences disturbed in endochondral bone formation in rickets are as follows: [39] The epiphyseal cartilage during normal growth exists as a narrow plate, supported by bone on the epiphyseal side

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36. Erdheim, J.: Rachitis und epithel Körperchen, Vienna, 1914.

37. Pappenheimer, A. M.: Experimental Rickets in Rats, J. Exper. Med. **36**: 335 (Sept.) 1922.

38. Hess, A. F.: Rickets, Including Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1930.

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and uniformly penetrated by blood vessels of capillary dimensions on the diaphyseal side. Very little evidence of growth is present on the epiphyseal side, where bone is closely applied in the form of transverse trabeculae or a thin fenestrated plate. Growth is accomplished by continuous proliferation of cartilage cells, arranged in columns, on the epiphyseal side, and simultaneous degeneration of the matured cells on the diaphyseal side. The cavities occasioned by the degeneration and disappearance of the cartilage cells at the diaphyseal end of the columns are entered by capillaries accompanied by cells (osteoblasts) which deposit osteoid on the exposed cartilage matrix; hence the first formation of bone is within spaces previously occupied by cartilage cells.

This behavior of the epiphyseal cartilage may be regarded as an ingenious device of nature in order to maintain a continuously retreating gap in the continuity of tissues, which is responded to by vascular outgrowth from the diaphyseal side, comparable to repair of any defect of tissues by the process of organization or granulation tissue formation. In normal growth there is, on the diaphyseal side of the narrow epiphyseal cartilage, a continuous layer of clear or empty cartilage cells, one or two cells deep. In normal growth, calcification of the cartilage matrix lateral to the columns of cells (so-called zone of provisional calcification) extends toward the epiphyseal extremity of the bone only as far as the cartilage cells are markedly degenerated. The first histologic evidence of rickets is the absence in whole or in part of the layer of clear (degenerated) cells and the consequent absence of ingrowth of capillaries. The matrix between the nondegenerated cartilage cells does not calcify. Slight degrees of rickets are manifested by a moderate increase in width of the epiphyseal cartilage presenting an irregular border on the diaphyseal side. This irregularity is due to the fact that the cessation of degenerative sequences in the cartilage cells does not take place simultaneously over the diaphyseal border. The width of the epiphyseal cartilage continues to increase because of the continued activity of the proliferative zone and the survival of the cells on the diaphyseal side. After cessation of the degenerative sequences of the cartilage cells and failure of cartilage matrix to calcify, osteoblasts in relation to the blood vessels in the diaphysis adjacent to the cartilage continue to deposit bone matrix or osteoid that does not calcify.

The degree or measure of severity of rickets may be gaged by the volume of the epiphyseal cartilage and amount of osteoid accumulated in the adjacent diaphysis, both expressions of degree and duration of retardation of two normal processes, one the cartilage sequence and the other, calcification of matrices.

In advanced rickets the noncalcified cartilage at the diaphyseal border becomes transversely stratified in places, evidently a mechanical effect of weight bearing. Osteoid material increases in amount with the duration of the deficiency and, being noncalcified, is molded by the stresses of weight and muscular efforts. Finally, there is disappearance of the cancellous bone of the diaphysis, marked resorption of cortical bone and deposition of subperiosteal osteoid. These are the factors that account for the deformities and fractures of bones in rickets.

Repair of Rickets.—The first histologic evidence of repair following corrections of the diet, either by amount of calcium and phosphorus or by administration of vitamin D, is the presence of cleared or degenerated cells on the diaphyseal border of the cartilage. Simultaneously, calcium is deposited in the cartilage matrix lateral to these cells. These effects are demonstrable at the end of twenty-four hours and are accompanied by extensive vascular responses, as shown by ingrowth of capillaries into empty cell spaces within forty-eight hours.

The first osteoid to be calcified in repair is that laid down in the resumption of normal sequences. The osteoid in the diaphysis that has accumulated during the deficiency subsequently becomes calcified and then is largely removed by osteoclasis. Repair proceeds rapidly in rats, even after severe rickets. From five to seven days suffices to restore the appearances of normal growth almost completely, though there is not complete removal of excess bone.

The osteomalacia of adults, when advanced, presents striking deformities of the skeleton and complicated microscopic pictures, all to be explained by loss of calcium salts in bone, secondary resorption of the matrix and new formation by way of reparative response of cells producing osteoid that does not calcify.

VITAMIN B COMPLEX

Present knowledge does not permit a rational account of the pathologic consequences of the deficiencies of what in the past has been called vitamin B or B complex. Vitamin B complex consists of a heat labile fraction, designated as B_1 and recently isolated in pure form, and a heat stable group. Claims by various authors have been made for as many as six different vitamins in the heat stable group, which is called vitamin B_2 or G. It is fairly certain now that this heat stable group contains probably no more than three vitamins: (1) lactoflavin, already isolated in pure form; (2) vitamin B_6, the absence of which in the diet of rats is responsible for a characteristic dermatitis affecting the extremities, nose, eyes and ears (this dermatitis has also been referred to as rat pellagra and B_6 as the antirat pellagra vitamin); (3) the pellagra preventing factor, which also prevents and cures black tongue in dogs.

It is not known whether pellagra and black tongue are due to the same deficiency, although the evidence is very strong that this is the case.

In the human being beriberi is a disease resulting from lack of vitamin B_1, but in all probability some of the features of this disease as commonly seen are due to other deficiencies. Those pathologic features which may be reproduced in pigeons by means of a diet adequate in all respects except in vitamin B_1 which are common also to human beriberi are some degree of enlargement of the heart, edema, atrophy of muscles, and degenerations of the nervous system. Manifestations of disorder of the nervous system are so striking that the condition in experimental animals is usually called polyneuritis. The conspicuous lesion is degeneration (Marchi degeneration) of the myelin sheaths of peripheral nerves; less certain are degenerative changes in ganglion cells of the brain, cerebellum, spinal cord and dorsal root ganglions. It must be remembered, however, that nervous symptoms appear late in the deficiency, and rats kept on vitamin B_1 deficiency may die without developing nervous lesions, so that a number of workers have questioned the specificity of degenerations of the myelin sheaths and have claimed to have produced the same degree of degeneration in

animals on a starvation diet in the presence of abundant vitamin B_1.[40] The consequences of starvation on the maintenance of myelin must be determined before the myelin sheath degenerations of this deficiency and other vitamin deficiencies (vitamin A and the heat stable fractions of B) can be attributed to a primary effect on the nervous system. Also of great importance in this connection is the fact that recovery from the nervous manifestations of experimental beriberi takes place in a very short time, and physiologic recovery results in a period of five or six hours following the administration of vitamin B_1.

I [41] could find no differences in the nerve lesions present in pigeons allowed to succumb with polyneuritis and those in which functional recovery had been induced by treatment. On the whole, it seems best to regard the primary pathologic effects of vitamin B_1 deficiency as not demonstrable at present and to regard all the pathologic changes thus far recorded, including the myelin sheath lesions, as secondary effects. The profound functional disturbances of the nervous system and speedy recovery, with treatment, do indicate that vitamin B_1 is directly concerned in the physiology of neurons. Also among the secondary consequences presumably due to disturbance in carbohydrate metabolism is enlargement of the islands of Langerhans in the pancreas, which I saw in experiments in 1925 and which have been reported by Ogata [42] and by Bierry and Kollmann.[43]

Similar difficulties are encountered in the consideration of the pathology of those conditions and diseases presumably resulting solely from deprivation of heat stable components of vitamin B. There is, for consideration, pellagra in the human being, black tongue in dogs, and rat pellagra or rat dermatitis or, as it is probably now preferably called, as suggested by Birch, György and Harris,[44] "rat acrodynia."

In pellagra, lesions of the nervous system are found but they are not pathognomonic in character. They are degenerative in type, in nerve cells and in myelin sheaths. In pellagra of long standing, lateral and posterior column degenerations in the spinal cord occur. Whether or not such extensive cord lesions have a pathogenesis (atrophy of the gastric mucosa) in common with those occurring in pernicious anemia remains to be solved. In dogs maintained on a diet deficient in the heat stable vitamin B complex (vitamin B_2 or G) extensive degeneration of the myelin sheaths also develop in peripheral nerves and tracts of the spinal cord.[45] Howe, Bessey and I [28] have been unable to obtain degeneration of the myelin sheaths in spinal cord or peripheral nerves in white rats maintained on a similarly deficient diet, even though they were carried to the point of death in the complete deficiency and for very long periods in partial deficiency. It must be concluded that the rat responds differently. The rats in our experiments did develop, as was to be expected, the skin lesions, or "rat acrodynia." That the factor preventing dermatitis in rats is different from that preventing the lesions of pellagra and black tongue has been proved.[44] It has been shown that diets producing pellagra in man and black tongue in dogs will cure the vitamin B_2 complex deficiency dermatitis of rats. Also, the dermatitis of rats is not influenced by light. We have found it to progress just as rapidly in rats kept in absolute darkness as in those kept in strong light. The distribution is also different and yet we are confronted with the paradox that histologically the lesions of the skin are very similar to those of pellagra and to the lesions of mucous membranes in black tongue of dogs. It is not advisable to describe in detail the histology of the skin lesions of rat dermatitis and of human pellagra. Careful study of rats made during the progress of the deficiency and in repair has failed to throw light on the initial effect in the skin, whether in the epidermis or in the underlying supporting tissues.

Until experiments on animals can be conducted with diets deficient only in single B factors, it would seem not worth while to attempt to characterize, pathologically, these deficiencies.

Until it is proved that the myelin sheath degenerations of the deficiencies are not simply starvation effects, the conclusion is warranted that the demonstrable nervous lesions of all the deficiency diseases are secondary effects and that no one vitamin is concerned in the maintenance of myelin. Lesions of skin and mucous membrane, such as have been described for pellagra, black tongue and rat dermatitis, are not common to deficiencies other than those found in the heat stable fraction of vitamin B or the vitamin B_2 complex, but it does not seem probable that the chemical mechanisms disturbed by the absence of the respective vitamins concerned will be found to occur primarily in the skin and mucous membranes. It may be said that the pathologic histology of pellagra, black tongue and vitamin B_2 or G deficiency in the rat, although presenting many interesting and suggestive features, is at present not more illuminating in regard to the mechanisms involved than are the sequences observed with the naked eye.

COMMENT

Our knowledge of the morphologic consequences of vitamin deficiencies is limited and has not extended beyond obvious tissue and cytologic changes.

The pathology of vitamin A deficiency indicates that the seat of the physiologic disturbances is in the epithelial cells. Chemical rôles are suppressed but proliferative powers are not inhibited; neither are the potentialities of cells lost, as is shown by the return to normal physiologic function when vitamin A is restored to the animal.

Vitamin C deficiency affects mesenchymal tissues, the most obvious morphologic consequence being the effect on the formation and maintenance of intercellular materials.

Vitamin D deficiency, besides the well known effect on calcium and phosphorus metabolism, suspends the cartilage cell cycle essential to endochondral growth of bone, though not impairing multiplication of the cartilage cells.

Vitamin B_1, as is indicated by recovery phenomena from the deficiency, must be more directly concerned in the physiology of the nervous system than is any

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other vitamin. The sudden return to normal function after administration of vitamin B_1, before morphologic repair has been initiated, warrants this conclusion.

A reasonable working hypothesis is that each vitamin is necessary in certain cells for one type of chemical mechanism the suppression of which is compatible.

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NEW FORMS AND SOURCES OF VITAMIN D

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Certain facts about vitamin D are widely known. It occurs only rarely in foodstuffs. It is formed in the skin by exposure to ultraviolet rays from the sun or from artificial sources. It is developed in some foodstuffs by their being briefly irradiated. It is produced by irradiating ergosterol, the sterol of fungi. From irradiated ergosterol it can be isolated and crystallized.

The fact that vitamin D is not a single chemical substance has only recently been recognized. The erroneous view still commonly held is that ergosterol is the parent substance, or provitamin, from which all vitamin D arises. Ergosterol exhibits four spectral absorption bands in the ultraviolet region. These bands were observed in the unsaponifiable fraction of the various materials that become antiricketic on irradiation. Since it is rare that even one band, not to mention such a series of bands, is exactly duplicated by different chemical substances, the evidence was misleadingly good that ergosterol was the one and only provitamin D.

I have reviewed elsewhere [1] in considerable detail the history of our knowledge of vitamin D, giving special attention to the experimental work on which its multiple nature is established. In a brief space, this can be recapitulated only in outline and brought up to date. So rapidly has investigation progressed that several new forms of vitamin D have been discovered within the past few months. One of these I shall describe for the first time.

The most thoroughly investigated form of vitamin D is that which results from the irradiation of ergosterol. This is known to physicians under trade names such as viosterol. The chemical name of the pure substance is calciferol. This particular form of vitamin D is also the form that is produced by irradiating yeast, the provitamin of which is ergosterol. It is thus the form that is present in the milk of cows to which irradiated yeast has been administered—the so-called yeast milk of commerce.

In our laboratory, in 1930, Massengale and Nussmeier [2] made the important discovery that the vitamin D of irradiated ergosterol and the vitamin D of cod liver oil act differently on rats and chickens. They found that, rat unit for rat unit, irradiated ergosterol is far less effective than cod liver oil for preventing rickets in chickens. Or, in other words, irradiated ergosterol is far more effective than cod liver oil, chick unit for chick unit, in preventing or curing rickets in rats.

This discovery, like several others in the field of vitamin D, was made simultaneously in more than one laboratory. Mussehl and Ackerson [3] and Hess and Supplee [4] came to the same conclusions from slightly different avenues of approach. It is recalled that Hess [5] and Steenbock [6] announced the discovery of activation within a few weeks of each other, that the provitamin concept was promulgated by three groups of investigators [7] Dec. 10, 1926, and that the high relative efficacy of irradiated 7-dehydro-cholesterol for chickens was reported by two independent groups [8] on the same day a few weeks ago.

The device of employing two species of test animals for assay purposes has come to be an extraordinarily useful tool in studies on the multiple nature of vitamin D. The knowledge that one species responds better to one form of this vitamin while another species responds better to another form has prompted investigators to compare the effectiveness of cod liver oil and irradiated ergosterol, rat unit for rat unit, on human beings. Differences have been claimed and denied. There is agreement to the extent that the difference, if any, is not large. Most of this work has been of poor quality, with groups of children so few in number and so diverse in age and background that the recorded observations are unimpressive to one who is familiar with the proper use and grouping of animals for the conduct of a biologic assay. Birds other than the common fowl, for example turkeys, respond like the common fowl, and mammals other than the rat, e. g., man, respond at least somewhat like the rat to these two kinds of vitamin D. It is therefore reasonable to expect that, if the number of species put to the test is extended, mammals in general will be found to respond well (per rat unit) to either irradiated ergosterol or cod liver oil, and birds in general will do poorly with irradiated ergosterol but will do well with cod liver oil.

The chemical constitution of the sterols is fairly well understood. The conventional numbering of the sterol ring, and the probable formulas of cholesterol, ergosterol and calciferol are shown in the accompanying structural formulas. From these concepts, the organic chemist has built several new vitamins D.

Windaus and Langer [9] added two atoms of hydrogen to the side chain of ergosterol at position 22. The new compound, 22-dihydro-ergosterol, gave by irradiation a new vitamin D, presumably 22-dihydro-calciferol. McDonald [10] has recently found that this slight molecular alteration increases by several times the effectiveness of the vitamin, per rat unit, for chickens.

From the Research Laboratory, Mead Johnson & Co.

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7. Rosenheim, O., and Webster, T. A.: Further Observations on the Photochemical Formation of Vitamin D, J. Soc. Chem. Ind. **45:** 932 (Dec.) 1926. Heilbron, I. M.; Kamm, E. D., and Morton, R. A.: The Absorption Spectra of Cholesterol and Its Possible Biological Significance with Reference to Vitamin D: I. Preliminary Observations, ibid. **45:** 932 (Dec.) 1926. Pohl, R.: Ueber das Absorptionsspektrum des antirachitisch wirksamen Cholesterins, Nachr. Ges. Wissensch. Goettingen, Math.-physik. Klasse, 1926, pp. 142-145.

8. (*a*) Bills, C. E.; Massengale, O. N.; Imboden, Miriam, and Hall, H.: The Multiple Nature of Vitamin D: II. The Vitamins D of Fish Oils, read before the American Institute of Nutrition, Washington, D. C., March 25, 1936. (*b*) Koch, Elizabeth M., and Koch, F. C.: The Antirachitic Actions of Irradiated Sterols and Derivatives Thereof, read before the American Institute of Nutrition, Washington, D. C., March 25, 1936.

9. Windaus, Adolf, and Langer, R.: Ueber das 22-Dihydroergosterin, Ann. **508:** 105-114 (Dec.) 1933.

10. McDonald, F. G.: The Multiple Nature of Vitamin D: III. Irradiated 22-Dihydroergosterol, read before the American Society of Biological Chemists, Washington, D. C., March 28, 1936.

Two years ago Waddell [11] made the surprising discovery that, in chicken-and-rat comparisons, irradiated cholesterol resembles cod liver oil and differs greatly from irradiated ergosterol, unit for unit. It occurred to Callow [12] and to me [1b] that by removing the methyl group at position 24 in the ergosterol side chain, in addition to introducing the hydrogen at position 22, a new provitamin D might be obtained which, on theoretical grounds, should give rise to a vitamin D simulating that of cod liver oil or, more particularly, of irradiated cholesterol. Such a provitamin would be a demethyldihydro-ergosterol, or, in terms of cholesterol, 7-dehydro-cholesterol. Windaus, Lettré and

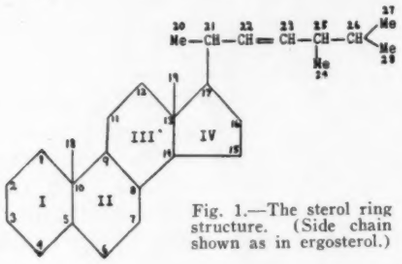

Fig. 1.—The sterol ring structure. (Side chain shown as in ergosterol.)

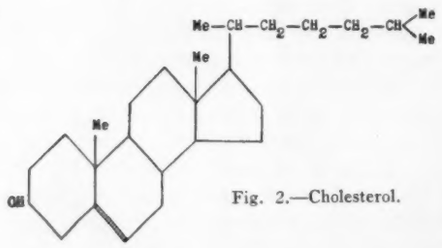

Fig. 2.—Cholesterol.

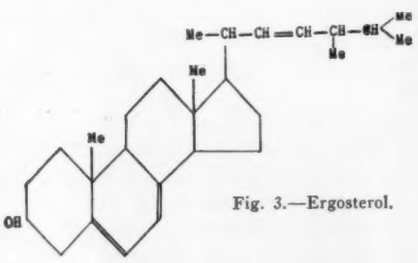

Fig. 3.—Ergosterol.

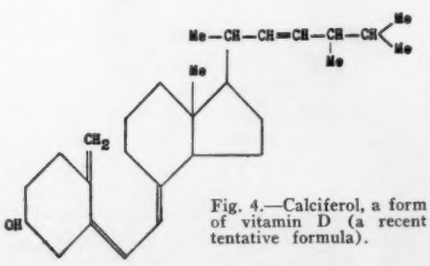

Fig. 4.—Calciferol, a form of vitamin D (a recent tentative formula).

Schenck [13] have synthesized this compound and found that, when irradiated, it gives a product effective in rat rickets. Repeating the synthesis, McDonald and I have confirmed the observations of the German workers and have substantiated the predictions by the discovery that, rat unit for rat unit, irradiated 7-dehydro-cholesterol is more effective than irradiated 22-dihydro-ergosterol and much more effective than irradiated ergosterol for chickens.[8a] The Kochs [8b] report similar results.

It was known that the activatability of cholesterol depended for the most part on its minute content of a provitamin, which had the same spectral absorption bands as ergosterol and which every one presumed to be ergosterol. These bands are also exhibited by 7-dehydro-cholersterol, and this fact, together with the behavior of the corresponding vitamin with chickens, suggests that 7-dehydro-cholesterol is the provitamin D in ordinary cholesterol. Many assays must still be carried out to establish whether 7-dehydro-cholesterol and the natural cholesterol provitamin, which are certainly similar, are actually identical. If they are identical, it probably follows that irradiated milk, which is activated by virtue of its cholesterol provitamin content, contains irradiated 7-dehydro-cholesterol and that this form of vitamin D, far from being a laboratory curiosity, is already an important practical source.

Another form of vitamin D was announced by McDonald [10] in March. This is irradiated 7-hydroxy-cholesterol or an impurity associated therewith. The absorption spectrum of 7-hydroxy-cholesterol is entirely different from that of the other provitamins D that I have mentioned. It consists of one rather wide band in place of the usual four, and general absorption in the far ultraviolet. In this connection, one recalls that cholesterol, specially treated to remove its ordinary provitamin, develops a new provitamin when heated.[14] The spectral absorption is general, no "ergosterol" bands being evident. It is thus possible that the provitamin developed by heating (with incidental oxidation) is 7-hydroxy-cholesterol or some similar substance.

It has been shown that the usual procedure (bromination, debromination) by which the ordinary provitamin is removed from crude cholesterol never completely destroys the activatability of the cholesterol.[15] Little is known of the residual provitamin, but Hathaway and Lobb [14] have recently reported that the vitamin D which results from irradiating it is much less effective, rat unit for rat unit on chickens, than the vitamin D produced by irradiating cholesterol which had first been purified and then heated to develop the new provitamin. In other words, this obscure form of vitamin D acts like calciferol, but since it is chemically impossible for it to be calciferol it must be recognized as still another kind of vitamin D.

The new vitamin D that McDonald and I announce at this time is prepared by irradiating a provitamin derived from sitosterol, the sterol of the higher plants which corresponds to cholesterol of animals. The provitamin is prepared by oxidizing sitosterol, reducing the oxidation product, treating the reduced material with benzoyl chloride in pyridine, and heating and saponifying the resulting ester. The procedure is similar to that used in preparing 7-dehydro-cholesterol. The provitamin exhibits a series of absorption bands and becomes antiricketic on exposure to ultraviolet rays.

Finally, I come to two forms of vitamin D that are produced by means other than irradiation. They have been known for some years, but only as curiosities. One of them supplied the first evidence of the multiple

11. Waddell, James: The Provitamin D of Cholesterol: I. The Antirachitic Efficacy of Irradiated Cholesterol, J. Biol. Chem. **105**: 711-739 (July) 1934.
12. Callow, R. K.: Vitamin D, Scient. J. Roy. Coll. Science **4**: 41-53, 1934.
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14. Koch, F. C.; Koch, Elizabeth M., and Ragins, Ida K.: Fractionation Studies on Provitamin D, J. Biol. Chem. **85**: 141-158 (Dec.) 1929. Koch, Elizabeth M.; Koch, F. C., and Lemon, H. B.: Absorption Spectra Studies on Cholesterol and Ergosterol, J. Biol. Chem. **85**: 159-167 (Dec.) 1929. Hathaway, M. L., and Koch, F. C.: Provitamin D Potencies, Absorption Spectra, and Chemical Properties of Heat-Treated Cholesterol, J. Biol. Chem. **108**: 773-782 (March) 1935. Waddell, James: Process for Producing Antirachitic Substances, U. S. Patent 2,028,364, Jan. 21, 1936. Hathaway, Milicent L., and Lobb, Dorothy E.: The Provitamin D of Heat-Treated Cholesterol, J. Biol. Chem. **113**: 105-110 (Feb.) 1936.
15. Bills.[1b] Koch, Koch and Ragins.[14] Bills, C. E.; Honeywell, Edna M., and MacNair, W. A.: Antiricketic Substances: VII. Biochemical and Spectroscopic Studies on Purified Cholesterol, J. Biol. Chem. **76**: 251-261 (Jan.) 1928.

nature of this vitamin. In 1926 McDonald and I [16] obtained a crude antiricketic product by treating cholesterol with a clay catalyst. We observed that this vitamin D, unlike the vitamin D of cod liver oil or irradiated cholesterol, was resistant to destruction by butyl nitrite. Yoder,[17] in reconsidering our reaction, suspected that the active principle involved was a derivative of the hydrocarbon cholesterilene. He found that cholesterilene sulfonic acid is a vitamin D, not very active to be sure, but extremely interesting to the chemist.

The other curiosity was described by us [18] in 1931. We found that ergosterol, when treated with nitrites, yielded an antiricketic derivative. Little is known of its chemistry, except that it differs from Yoder's product and also from any form of the vitamin that is not resistant to nitrites. Neither of these two forms of vitamin D has come into practical use, and we are reasonably certain that neither occurs in fish oils.

Thus we distinguish eight forms of vitamin D, and it seems probable that others can be produced. In fact, the number of possible forms may well be as many as the number of sex hormones which, as sterol derivatives, are chemically related to the vitamins D. The study of the effect of slight differences in molecular configuration on vitamin action has only just begun.

During the past ten years we have assayed the liver oils of about 130 species of fish, including nearly all which are of major importance commercially. A number of these were less potent than cod liver oil, but the majority were more potent. The oils of certain species, particularly the big percomorphs, exhibited from 100 to 1,000 times as much vitamin D per gram as cod liver oil, when assayed with rats. It occurred to us, in view of the numerous vitamins D prepared in vitro, that the vitamin D of these vastly different fish oils might vary in kind as well as in concentration.

We assayed the liver oils of twenty-five species of fish with both rats and chicks, finding, indeed, that the different oils varied greatly, rat unit for rat unit, in their effectiveness on chicks.[8a] The largest difference was observed between the oil of white sea-bass, Cynoscion nobilis, and certain species of tuna. The former was about twenty times as effective for chicks, per rat unit, as the latter.

Since it is inconceivable that each species of fish has its own private form of vitamin D, it must be concluded that any given fish oil probably contains at least two vitamins D, the proportions of which vary with the species. In other words, the vitamin D of fish oils can no longer be regarded as a single substance. It remains to be demonstrated which, if any, of the known forms of vitamin D occur in fish oils and whether any particular form is therapeutically more desirable than any other.

SUMMARY

Eight forms of vitamin D have been artificially prepared. At least two forms occur in fish oils, which may or may not be identical with certain of those made in vitro.

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17. Yoder, Lester: An Antirachitic Derivative of Cholesterol, Science **80**: 385-386 (Oct. 26) 1934. Yoder, Lester; Thomas, B. H., and Lyons, Malcolm: Experiments with a New Type of Antirachitic Substance, J. Nutrition **9**: (supp.) 6 (June 10) 1935 (abstract of meeting of April 10).

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THE PRESENT STATUS OF VITAMIN DEFICIENCIES IN PRACTICE

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It is becoming better and better recognized that the mild or latent forms of the vitamin deficiencies are more important in practice at present than the fully developed cases. The latter are uncommon, are easily recognized and are usually promptly and adequately treated. On the other hand there is reason to believe that minimal or mild forms of these diseases are much more frequent, often escape recognition and, because of their insidious effect on large numbers of people, constitute a more serious problem than the occasional advanced cases. It is true that the diagnosis of these mild forms is often difficult and uncertain. Nevertheless, there is available today much new knowledge of the vitamins which is applicable to the diagnosis and study of the milder forms of their deficiencies in patients. It is my purpose in this paper to describe the present means of diagnosis of the mild or early forms of each of the avitaminoses and to discuss briefly their incidence and certain aspects of treatment. No attempt will be made to present all the signs, symptoms or diagnostic procedures, even though they are present in the early and mild forms, my purpose being to select those which are most suitable, reliable and specific. Neither will it be possible to give a complete description of methods and technic in all cases. Because of the limitations of my experience, my remarks will deal principally with these disorders as they occur in adults.

A general statement regarding the incidence of these diseases should be made. In any given practice it will vary with the geographic location and with the economic status, age, sex and occupation of the patients. These, however, are factors that are of greatest importance in the primary or idiopathic forms of these diseases. Because of the probably high incidence of mild avitaminoses as complications of other disease, they must be of vital interest to all physicians irrespective of the nature of their practices.

VITAMIN A

Avitaminosis A is generally considered to be rare in this country, particularly among adults. For example, only four or five cases of xerophthalmia in adults have been reported in this country,[1] and in a recent questionnaire the number of cases of outspoken night blindness reported by a group of ophthalmologists was very small.[2] However, these are manifestations of severe A deficiency and do not measure at all adequately the incidence of the milder forms of this disease. Using newer methods of diagnosis, Jeans and Zentmire [3] recently reported forty-five cases of probable mild deficiency among a group of 213 children. In a more recent paper [4] the same authors found from 26 to 75

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Read before the Section on Pathology and Physiology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 14, 1936.

1. Thorson, J. A.: Nutritional Xerophthalmia, J. A. M. A. **103**: 1438 (Nov. 10) 1934.

2. Hess, A. F., and Kirby, D. B.: Incidence of Xerophthalmia and Night Blindness in the United States: Gage of Vitamin A Deficiency, Am. J. Pub. Health **23**: 935 (Sept.) 1933.

3. Jeans, P. C., and Zentmire, Zelma: Clinical Methods for Determining Moderate Degrees of Vitamin A Deficiency, J. A. M. A. **102**: 892 (March 24) 1934.

4. Jeans, P. C., and Zentmire, Zelma: The Prevalence of Vitamin A Deficiency Among Some School Children, J. A. M. A. **106**: 996 (March 21) 1936.

per cent of children of different social groups with evidence of A insufficiency. Park [5] examined a large number of subjects, both adults and children, some supposedly normal and others suffering from different diseases, and found evidence of a mild deficiency in a considerable number. The work of Frandsen,[6] although

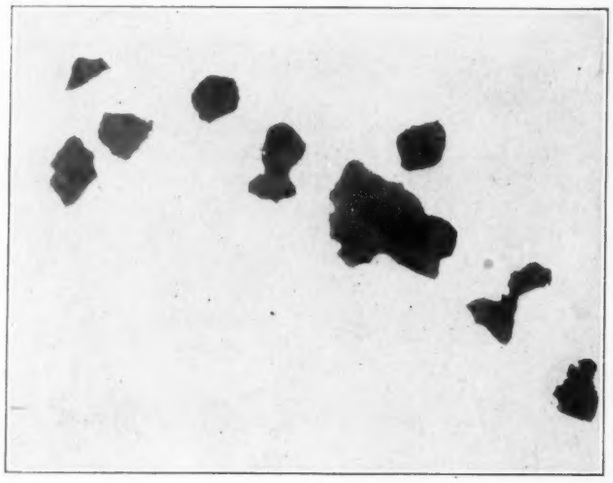

Fig. 1.—Smear from the bulbar conjunctiva of a white housewife, aged 52, who complained of vague pains in the arms, poor vision, pain and burning in the eyes and slight photophobia. There is marked cornification of all the cells.

done in Denmark, suggests that even in this country many more cases of mild vitamin A deficiency exist, both in children and in adults, than are recognized at present.

The earliest and the most reliable evidence of slight vitamin A deficiency is mild hemeralopia or a slightly lowered dark adaptation. The recent work of Jeans and Zentmire [7] and of Frandsen [6] seems to have demonstrated conclusively that clinically this symptom is most often a result of vitamin A deficiency and that it is often present long before other manifestations of the disease present themselves. In its earliest stages it may exist without the patient's knowledge or the patient may recall or recognize the symptom only after questioning. The abnormality may be detected by the use of the Birch-Hirschfeld photometer [8] or by the more simple apparatus described by Edmund and Ulrich Möller [9] and used by Helga Frandsen [6] in her study.

A second test consists of making a smear from light scrapings of the bulbar conjunctiva.[10] When properly stained, the presence of cornified epithelium indicates a deficiency of vitamin A (figs. 1 and 2). Sweet and K'ang [11] believe that this offers one of the most reliable methods of early diagnosis, though it is probable that in many cases hemeralopia precedes the changes in the conjunctiva. Nasal scrapings also may show a cornification of the epithelium. Asthenopia, poor vision, photophobia, Bitot's spots, conjunctival complaints and a dryness and granular appearance of the bulbar conjunctivae when the lids are held open for a few minutes occur as early manifestations of A deficiency and, while not specific, should arouse suspicion and lead to further tests.

The specific lesions in the skin have been only recently described [12] and are not widely known. They consist of keratotic papules of varying size, distributed especially over the thighs, arms and shoulders, surrounding and arising from the pilosebaceous follicles. Microscopically the ducts are distended and the openings are plugged with masses of cornified epithelium. There is atrophy of the glands and hyperplasia of the epidermis. The eruption is more common in adults and is said to be rare in children, which is of some diagnostic importance. In a fully developed form the eruption probably represents a late or severe deficiency. However, less extensive eruptions may occur in the milder forms, and I have observed two patients with papular lesions of this nature which disappeared after treatment with cod liver oil (figs. 3, 4, 5 and 6). Recently Scheer and Keil [13] have reported that the papules of vitamin C deficiency in the earlier or milder cases may resemble very closely those of vitamin A lack and have suggested the combined use of the capillary resistance test and biopsy in diagnosis. In all cases of vitamin A deficiency, confirmation of the diagnosis may be obtained by the result of adequate treatment with vitamin A, the changes in the eye particularly responding promptly to this measure.

VITAMIN B_1

The frequency of mild vitamin B_1 deficiency in this country is hard to estimate, though an endemic form

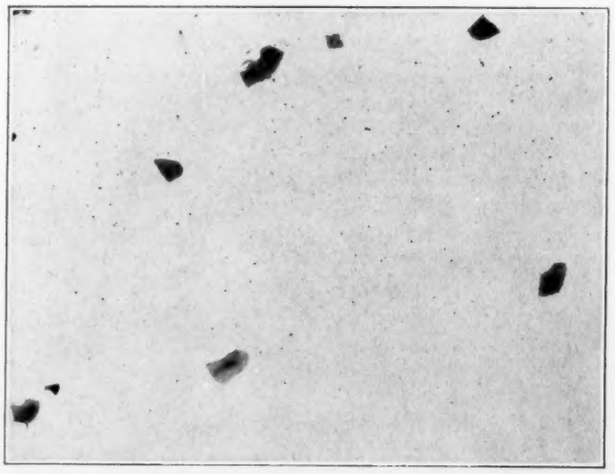

Fig. 2.—Smear from the same patient as in figure 1 after two weeks' treatment with cod liver oil. Many of the cells now are nucleated and show a return toward normal.

exists in Louisiana [14] and sporadic cases of beriberi or beriberi-like diseases are occasionally reported. Recent studies indicating that so-called alcoholic neuritis,[15] the

5. Park, I. O.: Preliminary Observations on Vitamin A Deficiency as Shown by Studies with Visual Photometer, J. Oklahoma M. A. **28:** 357 (Oct.) 1935.

6. Frandsen, Helga: Hemeralopia as Early Criterion of A-Avitaminosis and Clinical Symptoms and Treatment of This Disease, Acta. ophth. (supp. IV) 1, 1935.

7. Jeans and Zentmire (footnotes 3 and 4).

8. Birch-Hirschfeld, A.: On Night Blindness in War, Arch. f. Ophth. **92:** 273, 1917.

9. Edmund, C., and Möller, H. U.: Vision in Light of Reduced Intensity, Arch. Ophth. **54:** 531 (Nov.) 1925.

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11. Sweet, L. K., and K'ang, H. J.: Clinical and Anatomic Study of Avitaminosis A Among the Chinese, Am. J. Dis. Child. **50:** 699 (Sept.) 1935.

12. Frazier, C. N., and Hu, C. K.: Cutaneous Lesions Associated with Deficiency in Vitamin A in Man, Arch. Int. Med. **48:** 507 (Sept.) 1931. Loewenthal, L. J. A.: A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency, Arch. Dermat. & Syph. **28:** 700 (Nov.) 1933. Goodwin, G. P.: A Cutaneous Manifestation of Vitamin A Deficiency. Brit. M. J. **2:** 113 (July 21) 1934.

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14. Scott, L. C., and Herrmann, G. R.: Beriberi in Louisiana, J. A. M. A. **90:** 2083 (June 30) 1928.

15. Strauss, M. B.: The Etiology of "Alcoholic" Polyneurtis, Am. J. M. Sc. **189:** 378 (March) 1935. Jolliffe, N. H.; Colbert, C. N., and Joffe, P. M.: Observations on the Etiologic Relationship of Vitamin B (B_1) to Polyneuritis in the Alcoholic Addict. Am. J. M. Sc. **191:** 515 (April) 1936.

polyneuritis of pregnancy,[16] and other forms of peripheral neuritis[17] are in fact B_1 deficiency neuritis add additional groups of disorders to those caused by lack of this vitamin. Vorhaus, Williams and Waterman[17] have recently offered a clinical classification of B_1 deficiencies which includes a group with less specific

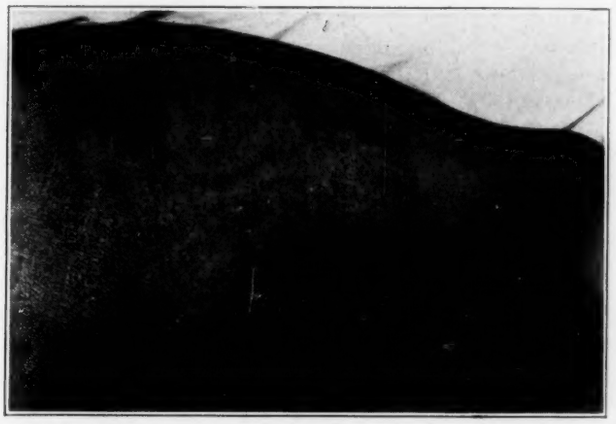

Fig. 3.—Papular lesions on the thigh of a Negress, aged 46, who complained of bronchitis, "pains all over," swelling of the feet, nervousness, weakness and anorexia.

symptoms such as anorexia, vague pains, weakness, indigestion and hypotonicity of the bowel (x-ray). If, as seems probable, such conditions are to be included, mild cases of the disease are common.

No conclusive symptom, sign or diagnostic test of minimal vitamin B_1 deficiency exists so far as I am aware. However, two procedures have recently become available which, together with symptoms suggestive of the disease, are helpful in diagnosis. The first is a calculation of the adequacy of the vitamin B_1 intake according to Cowgill's formula.[18] Jolliffe, Colbert and Joffe[15] have recently applied Cowgill's formula with great success in cases of so-called alcoholic neuritis. The second is the therapeutic test of giving the purified vitamin. The latter is, or will shortly be, available in a form suitable for parenteral administration. Unfortunately the signs and symptoms that would be expected to respond to this treatment are not specific and many of them are said to be caused by other vitamin deficiencies. Therefore, the absence of complete relief by adequate treatment does not preclude the presence of some avitaminosis B_1.

VITAMIN B_2 (G)

The evidence with respect to the frequency of mild B_2 deficiency is much more convincing than in the case of B_1. Assuming that pellagra is due to a deficiency of this factor, the condition is endemic in many parts of the South, and mild or early cases are common. More and more sporadic cases of pellagra are reported from other regions[19] and the existence of many mild or incomplete forms of the disease seems very probable.

Except for the dermatitis, the available means for the diagnosis of mild vitamin B_2 deficiency (pellagra) are no more satisfactory than in the case of B_1 deficiency. To the pellagra-conscious physician the presence of even slight changes in the skin consistent with the early dermal lesions of pellagra are sufficient to arouse a suspicion of the disease, as are the less specific symptoms of glossitis, diarrhea, digestive disturbances, and nervous and mental disorders. In addition to these symptoms there remains only a study of the diet and the therapeutic test, which in mild cases may be done by giving autoclaved yeast or, better still, the more potent liver extract, which may be given parenterally to avoid difficulties in absorption. Knowledge of the possible effects of deficiency of the other components of the B complex is still too incomplete to warrant a discussion of their clinical aspects.

VITAMIN C

Frank scurvy in adults is undoubtedly not common in most countries, though sporadic cases are occasionally reported, and it is found somewhat more frequently in children. In contrast, mild or latent scurvy or, better, a slight deficiency of vitamin C is probably very common. Harris and Ray,[20] using the newer clinical tests, found a number of children and adults who gave evidence of this condition, and many individual cases have been reported by others. My associates and I[21] found evidence of a mild insufficiency of vitamin C in twelve of fifteen adults whose diets were suspected of being inadequate in this factor. More significantly, of

Fig. 4.—Section of skin from the same patient as in figure 3, showing the hair follicle filled with a mass of keratinized débris.

a group of sixteen presumably normal subjects selected for controls eight were found to have evidence of this deficiency.

The recent isolation, identification and synthesis of vitamin C[22] (cevitamic acid) have made it possible to

16. Plass, E. D., and Mengert, W. F.: Gestational Polyneuritis, J. A. M. A. **101**: 2020 (Dec. 23) 1933. Strauss, M. B., and McDonald, W. J.: Polyneuritis of Pregnancy, ibid. **100**: 1320 (April 29) 1933. Greenhill, J. P.: Trends in Gynecology and Obstetrics During 1933, Am. J. Obst. & Gynec. **28**: 461 (Sept.) 1934. Fouts, P. J.; Gustafson, G. W., and Zerfas, L. G.: Successful Treatment of a Case of Polyneuritis of Pregnancy, ibid. **28**: 902 (Dec.) 1934.

17. Vorhaus, M. G.; Williams, R. R., and Waterman, R. E.: Studies on Crystalline Vitamin B_1; Experimental and Clinical Observations, J. A. M. A. **105**: 1580 (Nov. 16) 1935.

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19. Spies, T. D.: Treatment of Pellagra, J. A. M. A. **104**: 1377 (April 20) 1935.

20. Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin C Subnutrition by Urine Analysis, Lancet **1**: 71 (Jan. 12) 1935.

21. Youmans, J. B.; Corlette, M. B.; Akeroyd, J. H., and Frank, Helen: Studies of Vitamin C. Excretion and Saturation, Am. J. M. Sc. **191**: 319 (March) 1936.

22. Zilva, S. S.: The Isolation and Identification of Vitamin C, Arch. Dis. Child. **10**: 253 (Aug.) 1935.

study the excretion of this vitamin and its content in the tissues and body fluids. Although a final decision regarding normal values must wait until optimum requirements under various conditions have been determined, three possible methods for determining an inadequate intake, or store of vitamin C in the body, are available. These are (1) determinations of the daily excretion (urine), (2) a test of the body store ("saturation" or "retention" test) and (3) a determination of the amount of vitamin present in the blood plasma or serum.

Fig. 5.—Papular lesions in a diabetic girl, aged 20.

The amount of vitamin C in the urine is determined by a simple titration method using various indicators, the most useful clinically being dichlorophenolindophenol.[20] Because single specimens vary greatly in their content, the twenty-four hour excretion must be measured. Specimens may be examined singly during the twenty-four hours or the twenty-four hour specimen, suitably preserved, may be used. The method is sufficiently simple for office use and is, in fact, less trouble than the quantitative estimation of dextrose in the urine. As a result of our studies we[21] have tentatively adopted an excretion of 20 mg. a day as the lower limit of normal excretion under usual circumstances. It should be emphasized that this does not necessarily represent an optimum state under any or all conditions.

The "saturation" or "retention" test[20] is performed by giving a large amount of vitamin C (600 mg. in adult) either as pure cevitamic acid or as orange juice, and determining the excretion in the urine in the twenty-four hour period during which the test dose is administered. In patients with a poor store of vitamin C the greater part of the test dose is retained (little is excreted), while in those with a good store a large part is eliminated. While final standards have not been set, my associates and I have taken the excretion of at least 30 per cent of such a test dose as the lower limit of normal under ordinary conditions in an adult[21] (fig. 7).

Finally, the amount of vitamin C in the blood plasma or serum may be determined. Normal values have not been finally established and will vary, depending on whether total or reduced cevitamic acid is determined according to the method used.[23] Farmer and Abt[23] found from 1.030 to 2.29 mg. per hundred cubic centimeters of reduced cevitamic acid in adults, and from 0.819 to 1.374 mg. in children whose diets were believed to be satisfactory. The same authors found 0.687 and 0.917 mg. in two adults and 0.458 and 0.617 mg. in two children whose diets may have been deficient. In normal subjects on a usual or forced intake of vitamin C my associates and I, using a similar method, have found values of from 1.66 to 4.31 mg. per hundred cubic centimeters. In twelve patients whose diets were suspected of being low in vitamin C, some of whom showed signs and symptoms compatible with mild vitamin C deficiency, the values ranged from 0.254 mg. to 1.09 mg., with an average of 0.539 mg. However, the intake of even moderate amounts of vitamin C causes a quick, though temporary, rise in the blood. Furthermore, with a low vitamin C intake, for even a short period, the concentration in the blood falls to a relatively low level, though there is a good store in the body and no evidence of a deficiency.[24] Obviously, both these factors must be taken into consideration in interpreting values found on examination of the blood.

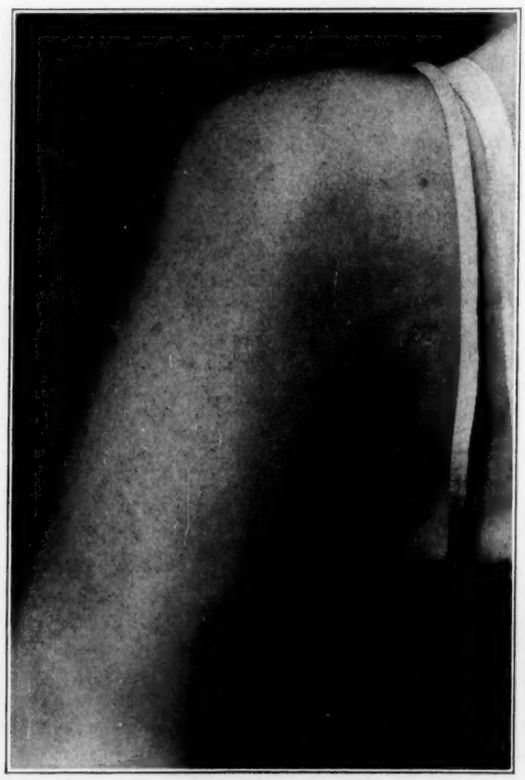

Fig. 6.—Same area as shown in figure 5 after six weeks' treatment with cod liver oil.

23. Mirsky, I. A.; Swadesh, S., and Soskin, Samuel: Total Ascorbic Acid Content of Human Blood, Proc. Soc. Exper. Biol. & Med. **32**: 1130 (April) 1935. Farmer, C. J., and Abt, A. F.: Ascorbic Acid Content of Blood, ibid. **32**: 1625 (June) 1935.

24. Youmans, J. B., and associates: Unpublished data, 1936.

Besides these tests there is the test of capillary resistance. This procedure, as modified by Göthlin,[25] consists of counting the number of petechial hemorrhages that appear in an area of skin of 60 mm. diameter in the antecubital fossa, after fifteen minutes of venous stasis with a blood pressure cuff at a pressure of 50 mm. of mercury. The appearance of more than eight is considered positive, of less than five negative. Although not specific, the results of such a test have been found to correspond well to the probable state of vitamin C intake and store and the therapeutic administration of the vitamin.[25] In the absence of other causes for such hemorrhages, a positive test is strong evidence of a vitamin C deficiency.

VITAMIN D

Vitamin D deficiency appears to be uncommon in adults and occurs sporadically mainly as a complication in diseases that interfere with the absorption of food.

In children the presence of a deficiency in vitamin D may be readily shown by the presence of characteristic lesions in the long bones, as seen in roentgenograms. In the adult no satisfactory clinical test exists and in any question of vitamin D deficiency there is involved the problem of calcium, phosphorus and parathyroid hormone metabolism as well. Deficiency of vitamin D is to be suspected when the diet appears to be lacking in the vitamin, or in the presence of such conditions as osteoporosis, osteomalacia, tetany and insufficiently explained fractures. It is particularly to be looked for in the presence of conditions that lead to a greater demand for this vitamin, such as pregnancy or lactation, or in diseases that interfere with its absorption and utilization, such as celiac disease, chronic jaundice and external biliary fistula. In suspected cases the effect of adequate treatment with the vitamin may be helpful diagnostically.

VITAMIN E

Too little is known of the clinical effects of vitamin E deficiency to warrant an extended discussion of its frequency or diagnosis. The vitamin is held so tenaciously by the tissues, the source is so varied and the supply so abundant that deficiencies are probably rare. There is evidence,[26] however, that some cases of functional sterility and habitual abortion are caused by a lack of this vitamin and in such cases this deficiency is to be suspected.

From this review of the incidence and diagnosis of the avitaminoses it may be concluded that all who are engaged in practice must be conscious of the existence of these disorders and alert to detect them. Because these deficiencies occur not only as independent diseases but perhaps even more often as complications of other diseases, this applies not only to the physician in general practice and the internist but to every specialist as well. Any patient whose intake of food is restricted from any cause, or in whom there is any interference with its absorption or utilization, or whose need for the vitamins is increased should be examined critically for the possible presence of a vitamin deficiency.

One's suspicions having been aroused, the further steps in study, diagnosis and treatment may be outlined briefly as follows: First, a careful scrutiny of the diet. I would emphasize the necessity for careful and detailed, often minute, inquiry. The importance of the quantitative factor in diets alone makes this necessary. Much too often in the past, physicians have been satisfied with a few cursory questions. I have found it helpful to have the patient record the kind and amount of food eaten over a period of a week or more. While errors are possible with this method, it has proved a valuable aid in diagnosis, and I have frequently been astonished at the dietary deficiencies it has disclosed. It is also useful as a basis for further questioning at a subsequent visit.

The second step is to test by such methods as those just described for the presence of the various vitamin deficiencies. Because of the frequency of multiple deficiencies and the similarity of the symptoms produced by them, particularly in mild deficiency states, it will often be necessary to test for the presence of several deficiencies, though symptoms and a consideration of the diet may indicate that which is probably preponderant.

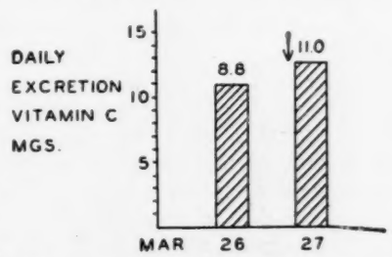

Fig 7.—Daily excretion of vitamin C and result of saturation test in a woman, aged 61, with edema, hypoproteinemia, gingivitis and dermatitis; 600 mg. of vitamin C was given at the point marked by the arrow without any significant increase in the daily excretion.

The third step is treatment with the specific substances. This may also be of considerable diagnostic importance. In treatment a number of factors may influence the response and hence are important diagnostically and therapeutically. When the therapeutic test is used, the preparations should be as pure as possible. Because of multiple deficiencies, treatment with several of the vitamins may be necessary and it may be helpful to administer them successively. The factor of dosage is of great importance, particularly in treatment or cure as contrasted with prevention. This is especially true when the avitaminoses complicate other diseases, when there is interference with absorption and utilization, or an increased demand. When absorption by the usual routes is hindered, administration should be by routes that insure absorption. In prophylaxis, in very mild deficiencies or to maintain a cure, considerations of economy and palatability, as well as common sense, indicate the use of natural foodstuffs. In these circumstances, however, it will be necessary to insure availability, proper preparation of food, and the continuance of an adequate intake.

At the present time no pure or injectable preparations of vitamin A are available and for administration the richest preparations are certain fish oils. Carotene, the precursor of vitamin A, may be given, even parenterally, but the evidence of Drummond, Bell and Palmer [27] would suggest that under many conditions

25. Göthlin, G. F.: Outline of a Method for the Determination of the Strength of the Skin Capillaries and the Indirect Estimation of the Individual Vitamin C Standard, J. Lab. & Clin. Med. **18:** 484 (Feb.) 1933.
Other modificatons are described by:
Falk, G.; Gedda, K. O., and Göthlin, G. F.: An Investigation into the Strength of the Skin Capillaries and Indirectly into the Vitamin C Standard of School Children in the District of Norrbolten, North of the Arctic Circle, Skandinav. Arch. f. Physiol. **65:** 24, 1932.
Dalldorf, Gilbert: A Sensitive Test for Subclinical Scurvy in Man, Am. J. Dis. Child. **46:** 794 (Oct.) 1933.
Greene, David: Evaluation of the Capillary Resistance Test in the Diagnosis of Subclinical Scurvy, J. A. M. A. **103:** 4 (July 7) 1934.
Molith, Mathew, and Cousins, R. F.: Subclinical Scurvy in Children, J. Lab. & Clin. Med. **21:** 43 (Oct.) 1935.
Wright, I. S., and Lilienfeld, Alfred: Pharmacologic and Therapeutic Properties of Crystalline Vitamin C (Cevitamic Acid), Arch. Int. Med. **57:** 241 (Feb.) 1936.

26. Watson, E. M.: Clinical Experiences with Wheat Germ Oil (Vitamin E), Canad. M. A. J. **34:** 134 (Feb.) 1936.

27. Drummond, J. C.; Bell, M. E., and Palmer, E. T.: Observations on Absorption of Carotene and Vitamin A, Brit. M. J. **1:** 1208 (June 15) 1935.

vitamin A is to be preferred to carotene because the former is better absorbed by mouth.

Vitamin D is available in concentrated form, and large doses may easily be given by mouth or through the skin. Only in the case of this vitamin does there appear to be any danger of inducing a hypervitaminosis. The toxic dose is so large, however, that this danger is encountered only rarely. The symptoms of early hypervitaminosis D have been summarized by Bills.[28]

The need for vitamin B_1 is affected by so many factors that it seems unwise to set any single amount as the minimum requirement, and little is known about the optimal supply. Vorhaus, Williams and Waterman[17] believe that the minimum daily therapeutic dose that can be relied on to abolish any accumulated deficit and supply current needs is 10 mg. of the pure material. Vitamin B_1 will soon be available commercially in pure crystalline form, injectable and hence of value in ensuring adequate intake and certain absorption. However, because other fractions of the vitamin B complex may be concerned in the production of symptoms, it may often be advisable in treatment to employ more complex products, such as the concentrated yeast and wheat germ preparations.

In pellagra, Spies[19] has shown that energetic treatment by diet, symptomatic measures and the administration of large doses of vitamin preparations, including liver extract or ventriculin, orally or parenterally, will greatly reduce the mortality in even desperate cases. The need for intensive treatment varies with the severity of the illness, and mild cases will permit the use of specific substances alone when a therapeutic test is desired. Subsequent control of the diet is important to prevent relapses, especially in cases in which there are difficulties in absorption.

Pure vitamin C (cevitamic acid) is now available at prices that compare favorably with orange juice. Minimum protective doses are usually considered to be in the neighborhood of from 25 to 40 mg. daily, but knowledge of the occurrence of mild deficiencies suggests that this amount should be larger and optimal amounts considerably greater. When necessary, pure vitamin C may be given intravenously if precautions are taken to neutralize it when large doses are given. When vitamin C is administered in the form of fruit juice the vitamin content should be determined, especially in the case of canned juice, some brands of which contain practically no vitamin C.[29] Natural juice also varies in its potency, and caution should be taken to avoid loss by standing.

It is to be feared that the frequency of these disorders, the presence of multiple deficiencies in many cases and the absence of clear cut signs or symptoms in the milder forms will foster careless and incomplete diagnosis and the complacent acceptance of such general terms as "deficiency disease," "multiple avitaminosis" and the like. This attitude will in turn lead to the uncritical use of complex mixtures in treatment.[30] Such a practice is no more justified than failure to diagnose other diseases accurately. One might as consistently make a diagnosis of heart disease and give digitalis, glyceryl trinitrate, diuretics and thyroid extract, without attempting to determine the etiology, pathologic changes and functional disorders. The only proper procedure in every case of suspected vitamin deficiency is to determine the nature of the deficiency and the pathologic and functional changes resulting from it, as completely as possible. In this way the clinician not only insures accurate, complete diagnosis and proper treatment but is able to contribute to our knowledge of the vitamins as they relate to human health.

28. Bills, C. E.: Physiology of Sterols, Including Vitamin D, Physiol. Rev. **15**: 1 (Jan.) 1935.
29. Youmans, J. B.; Corlette, M. B.; Akeroyd, J. H., and Frank, Helen: A Clinical Study of Vitamin C Excretion, South. M. J. **29**: 37 (Jan.) 1936.
30. Shotgun Vitamin Therapy, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **105**: 1037 (Sept. 28) 1935.

SUMMARY

Briefly, the minimal forms of vitamin deficiencies are important problems in all forms of practice. Although diagnosis is more difficult in these cases, there are available methods which may be employed successfully in many cases, and every effort should be made to secure an early and accurate diagnosis. For the early diagnosis of vitamin A deficiency there is available a test of slight hemeralopia and the examination of smears from the bulbar conjunctivae. In vitamin B_1 deficiency states the adequacy of the vitamin intake may be calculated as a presumptive test, to be substantiated by the results of treatment with the pure vitamin. In mild vitamin B_2 deficiency, diagnosis depends on suggestive clinical symptoms, a study of the diet and the therapeutic results of relatively pure products such as autoclaved yeast and liver extracts. Slight degrees of vitamin C deficiency may be detected by urinalysis and the response to large test doses of the vitamin. The diagnosis of vitamin D deficiency in adults is difficult because of the complicating factors of calcium, phosphorus and parathyroid metabolism. At the present time vitamin E deficiency may be suspected only by the presence of clinical symptoms and a consideration of the diet. In most cases potent and concentrated preparations of the vitamins are available for critical and scientific treatment of these deficiency states.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. WOLBACH, BILLS AND YOUMANS

DR. ARTHUR F. ABT, Chicago: Dr. Chester J. Farmer and I have recently completed an investigation on the concentration of cevitamic acid (reduced) in the blood plasma in normal and abnormal states. By the use of a microchemical method devised by us, we have determined the reduced cevitamic acid content of the blood plasma in a group of infants and children on adequate vitamin C containing diets. No correlation between the age of the individual and the cevitamic acid content of the blood plasma could be demonstrated. Our results fail to substantiate the synthesis of cevitamic acid in infants. A definite correlation between blood plasma values and capillary skin resistance tests could not be demonstrated. Single determinations of cevitamic acid in the blood plasma are an accurate index for the detection of clinical scurvy. From our experience to date, we feel that the level (in milligrams per hundred cubic centimeters) of reduced cevitamic acid in a single blood sample taken on a fasting stomach is indicative of the tissue saturation. Blood tolerance curves and twenty-four hour urine excretion values bear out this opinion. In other words, if one wishes to investigate tissue saturation to determine whether there is a prevalence of subclinical scurvy or whether a number of children in any region are lacking in dietary vitamin C, single blood determinations will give the desired information. We now have a technic whereby, instead of puncturing a vein, we may take a few drops of blood from the finger or heel, which will yield an accurate value and which we feel is a much simpler method than taking twenty-four hour urine specimens. With the aid of the microchemical method, hourly blood determinations can be plotted. Our results indicate that the occurrence of congenital scurvy is possible. We feel that cevitamic acid blood plasma values are a better index in healing scurvy than tests for capillary skin resistance or serial

x-ray films of the long bones. Blood plasma values show a rapid rise in a healing scurvy, and a single blood determination is more informative than a single or twenty-four hour urinary determination. We conclude that the cevitamic acid (reduced) content of the blood plasma varies directly with the vitamin C content of the diet. If complete metabolism studies on vitamin C are to be made, absorption by the gastro-intestinal tract must be considered and it must also be recognized that there are other channels of excretion than the urine. It is already known that cevitamic acid is present in significant quantities in the saliva and the milk. Elimination through the gastro-intestinal tract must also be considered in diarrheal states, so common in infancy and childhood.

DR. S. B. WOLBACH, Boston: I should have explained what I meant by specific starvation. In vitamin A deficiency, for example, the cell in one sense is not starved; in fact, I think that the proliferative power of the epithelial cell as shown by its regeneration is increased, yet that cell is not able to do something it formerly did, and that is the connotation I wish to give to specific starvation, not cell hunger in the broad sense.

THE OLFACTORY BULBS IN EXPERIMENTAL POLIOMYELITIS

THEIR PATHOLOGIC CONDITION AS AN INDICATOR OF THE PORTAL OF ENTRY OF THE VIRUS

ALBERT B. SABIN, M.D.
AND
PETER K. OLITSKY, M.D.
NEW YORK

It has been repeatedly shown by many investigators [1] that when the virus of poliomyelitis is instilled intranasally in rhesus monkeys it enters the central nervous system by way of the olfactory nerves and bulbs. Our purpose in the present communication is to describe the pathologic changes produced by the virus in its passage through the olfactory bulbs and to present evidence that these changes occur only when the virus has reached the bulbs from the periphery by way of the olfactory nerves and not when the invasion of the central nervous system is by other pathways.

Experimental poliomyelitis in rhesus monkeys was produced almost constantly by instilling 1 cc. of a 10 per cent virus suspension (M. V. strain) into each nostril on one day and repeating the process forty-eight hours later. With this procedure the first rise of temperature occurs between the fourth and sixth days and paralysis first appears on the seventh to ninth days after the first instillation of virus. The olfactory bulbs were fixed in Zenker's fluid containing 5 per cent glacial acetic acid, embedded in paraffin, and sections cut at 5 microns were stained with phloxine and methylene blue. As a rule the entire bulb was embedded with the anterior pole downward, and transverse sections were obtained from at least four to six different levels.

The earliest examination was made on the fourth day after the first dose of virus. At this time the lesions were already present and involved several layers of the olfactory bulbs from without inward. The outer layer of olfactory nerve fibers and the adjacent layer of glomeruli were diffusely infiltrated with inflammatory cells, consisting of polymorphonuclear leukocytes, mononuclear cells and lymphocytes. Polymorphonuclear cells were also scattered through the lamina granulosa externa and the lamina gelatinosa, the layers between the glomeruli and the mitral cells. The large mitral cells, which at the glomeruli are in synaptic relation with the primary olfactory neurons situated in the nasal mucosa, showed advanced necrotic changes, while the smaller cells in the internal granular layer among which they lie appeared to be generally well preserved. Many of the mitral cells were reduced to structureless, acidophilic masses with pyknotic, shrunken nuclei, and some were undergoing neuronophagia. With these changes in the olfactory bulbs on the fourth day after instillation and approximately four days before the onset of paralysis the spinal cord still appeared normal, while lesions were already present in the diencephalon, mesencephalon and pons. In monkeys examined after the onset of paralysis or post mortem, further changes in the olfactory bulbs consisted of neuronophagia of the involved mitral cells and an increased inflammatory process in the peripheral layers where the blood vessels showed characteristic perivascular cuffing. With the exception of an occasional polymorphonuclear leukocyte, no lesions were seen in the center of the bulbs

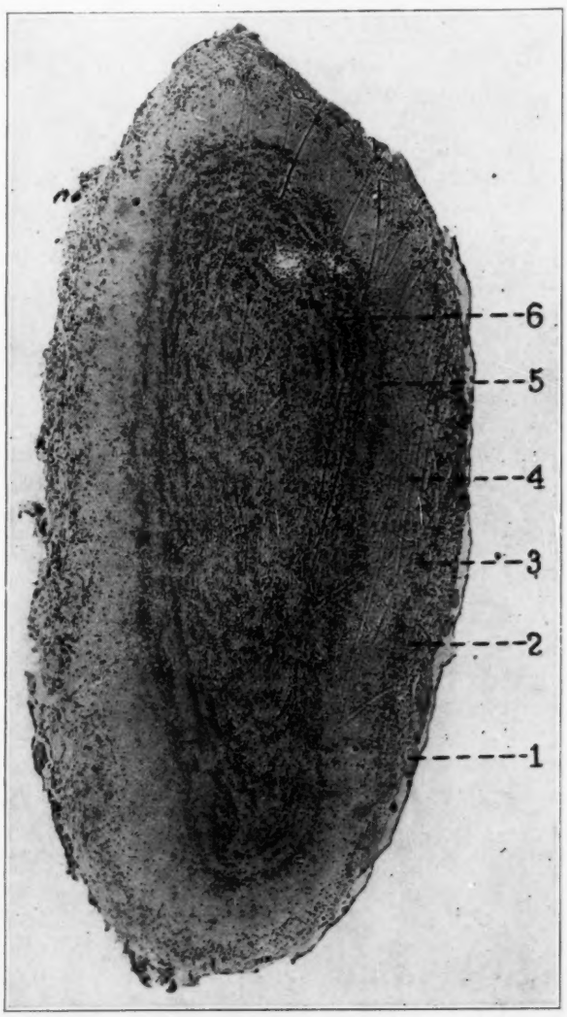

Fig. 1.—Transverse section of olfactory bulb of normal Macacus rhesus monkey: 1, lamina fibrorum nervi olfactorii; 2, lamina glomerulosa; 3, lamina granulosa externa; 4, lamina gelatinosa; 5, lamina cellularum mitralum; 6, lamina granulosa interna. × 40.

From the Laboratories of the Rockefeller Institute for Medical Research.

1. Flexner, Simon, and Clark, P. F.: A Note on the Mode of Infection in Epidemic Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **10**: 1, 1912. Faber, H. K., and Gebhardt, L. P.: Localizations of the Virus of Poliomyelitis in the Central Nervous System During the Preparalytic Period, After Intranasal Instillation, J. Exper. Med. **57**: 933 (June) 1933. Brodie, Maurice, and Elvidge, A. R.: The Portal of Entry and Transmission of the Virus of Poliomyelitis, Science **79**: 235 (March 9) 1934. Schultz, E. W., and Gebhardt, L. P.: Olfactory Tract and Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **31**: 728 (March) 1934.

beyond the layer of mitral cells. Intranuclear inclusions of the type described in experimental poliomyelitis [2] were not found in the bulbs even when examined on the fourth day, probably because necrosis had already advanced to too late a stage. That the method was suitable for demonstrating them is evident from the fact that they were observed elsewhere in the central nervous system.

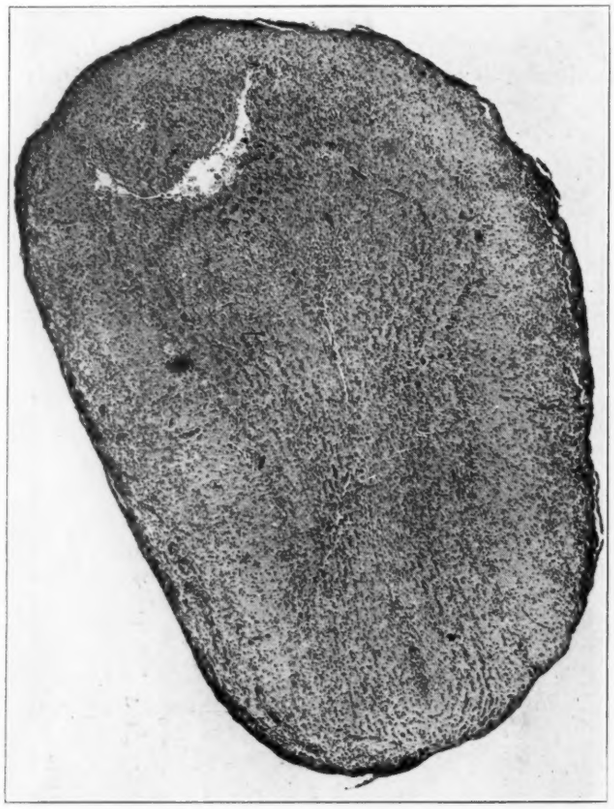

Fig. 2.—Transverse section of olfactory bulb four days after nasal instillation of poliomyelitis virus. At this magnification only the diffuse inflammatory reaction in the outer layers is perceptible. × 40.

The pathologic changes just described were found in the olfactory bulbs of each of the eighteen monkeys that had been infected by the intranasal route and examined for the most part at the termination of the disease. The type and extent of the lesions varied in individual animals. In some many mitral cells were destroyed, while in others only a few. The intensity of the peripheral inflammatory reaction did not appear to depend on the number of necrotic nerve cells, for it was marked in some bulbs with only a few damaged cells; in others the outstanding lesion was neuronophagia of many mitral cells, with little or no meningeal or perivascular reaction. Although the virus was instilled in both nostrils, one of the olfactory bulbs frequently showed more extensive lesions than the other, and in five of sixteen monkeys in which both bulbs were in suitable condition for adequate examination, only one of the two appeared to be involved. The unilateral involvement of the olfactory bulbs in almost a third of the number of animals under the present experimental conditions clearly points to the necessity of studying both bulbs in each instance.

2. Covell, W. P.: Nuclear Changes of Nerve Cells in Acute Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **27**: 927 (June) 1930. Hurst, E. W.: The Occurrence of Intranuclear Inclusions in the Nerve Cells in Poliomyelitis, J. Path. & Bact. **34**: 331 (May) 1931.

In order to throw more light on the nature and specificity of the described pathologic changes, it appeared desirable to study the olfactory bulbs of immune, convalescent monkeys resistant to nasal instillation of the virus suspensions. Four convalescent monkeys with residual paralysis that had previously been shown to be resistant to reinoculation were tested. Two of them had their primary infection by the nasal route three and one-half months, one by the intracerebral three and one-half months and another by the same route two and one-half months previously. After receiving virus intranasally, as a result of which control monkeys instilled simultaneously succumbed with poliomyelitis, they were killed two, four, five and seven days after instillation and their olfactory bulbs examined. None of the lesions just described were detected in any of them, thus yielding additional evidence that

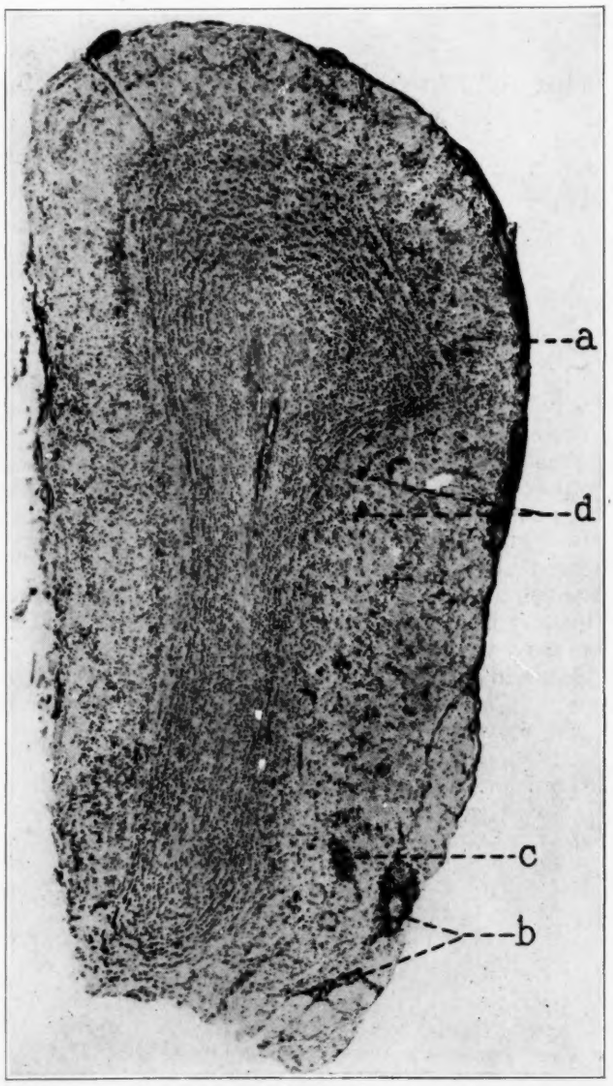

Fig. 3.—Transverse section of olfactory bulb of monkey succumbing to experimental poliomyelitis eight days after nasal instillation of virus. Note dense cellular infiltration at *a*, perivascular cuffing at *b*, aggregate of inflammatory cells in glomerular region at *c* and neuronophagia of mitral cells at *d*. × 40.

these pathologic changes are the result of active infection of the olfactory bulbs with the virus of poliomyelitis. It also became apparent that three and one-half months after infection by way of the nose the lesions observed during the acute stage may have disappeared, leaving evidence only of reparative changes.

That these pathologic changes may serve to indicate the portal of entry of poliomyelitis virus became evident from an examination of the olfactory bulbs of thirteen monkeys succumbing to the experimental disease induced by intracerebral, subcutaneous, intra-ocular and intrasciatic inoculation. Although the disease had been purposely allowed to run its full course in these monkeys, the olfactory bulbs appeared entirely normal. It is

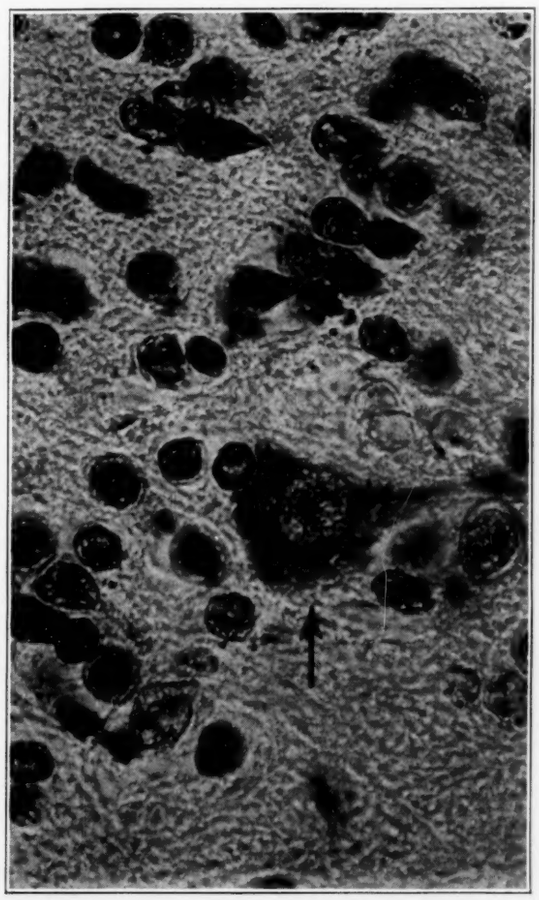

Fig. 4.—Mitral cell amid smaller cells of internal granular layer in normal olfactory bulb. × 1,000.

clear, therefore, that virus introduced directly into the brain or reaching the central nervous system by nerves other than the olfactory fails to induce the characteristic lesions in the bulbs. Recently it has been suggested by several investigators [3] that when large amounts of poliomyelitis virus are injected intravenously it may, after being eliminated on the nasal mucosa, invade the central nervous system by way of the olfactory nerves. The olfactory bulbs of three monkeys succumbing to poliomyelitis after intravenous injection of the virus were examined, and while typical lesions were found in one case there was none in the other two. These results indicate that virus from the blood stream can reach the central nervous system not only by way of the olfactory nerves but also by other pathways.

Although most investigators, and notably Flexner, believe that the nose is the natural portal of entry of the virus in man, others maintain that under certain conditions the gastro-intestinal route may supply the pathway for invasion of the virus. That postmortem examination of the olfactory bulbs can supply valuable data regarding this question is evident from the results presented in this communication. Yet, as stated by Faber [4] in his review of work done on poliomyelitis up to 1933, "Little or no attention appears to have been devoted to the pathology of the olfactory bulb in poliomyelitis. It is a familiar fact that, unless special care is observed, the olfactory bulb, firmly attached as it is by the numerous olfactory nerves, is likely to be torn off when the brain is removed at necropsy, and so fail to be examined. This is the only explanation that occurs to me for the uniform failure to note either the macroscopic or microscopic appearance of the structure in the protocols available in the literature. Harbitz and Scheel briefly note in one case that the olfactory bulb was normal—the only instance in which I have found it mentioned."

Since then only the work of L. W. Smith,[5] reported in 1934, has come to our attention. This investigator studied microscopically fifty-six olfactory bulbs from about forty cases [6] of human poliomyelitis and stated that this examination "has shown a surprisingly small

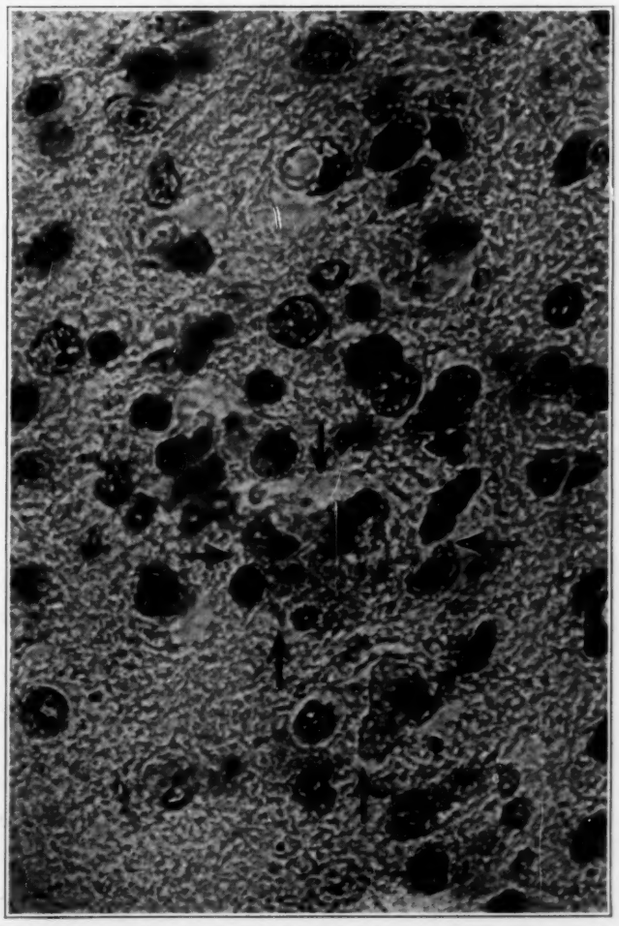

Fig. 5.—Mitral cell layer in olfactory bulb four days after nasal instillation of poliomyelitis virus. Note one necrotic mitral cell and another in an early stage of neuronophagia. × 1,000.

amount of pathological change. There has frequently been edema and congestion, harbingers of more extensive damage, but in less than a fourth of them do the

3. Lennette, E. H., and Hudson, N. P.: Relation of Olfactory Tracts to Intravenous Route of Infection in Experimental Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **32**: 1444 (June) 1935. Armstrong, Charles: Prevention of Intravenously Inoculated Poliomyelitis of Monkeys by Intranasal Instillation of Picric Acid, Pub. Health Rep. **51**: 241 (March 6) 1936.

4. Faber, H. K.: Acute Poliomyelitis as a Primary Disease of the Central Nervous System, Medicine **12**: 83 (May) 1933.

5. Smith, L. W., in Landon, J. F., and Smith, L. W.: Poliomyelitis: A Handbook for Physicians and Medical Students, Based on a Study of the 1931 Epidemic in New York City, New York, Macmillan Company, 1934, p. 50.

6. Smith, L. W.: Personal communication to the authors.

characteristic cellular infiltrative changes, as seen in the ganglia and nerve roots, appear. Either any inflammatory reaction in these organs is extremely short lived, unlike the lesions of poliomyelitis elsewhere in the central nervous system, or the virus passes along these structures without leaving its identifying signature. A third possibility, which strikes us as more logical, in view of the essential difference in the nature of the pathological lesions, is that the olfactory bulb in human beings is not necessarily as frequent a pathway for the

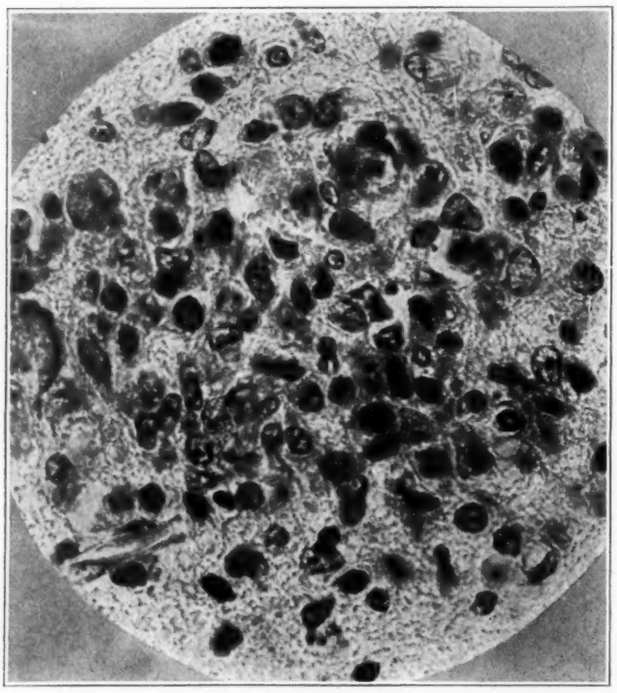

Fig. 6.—Advanced neuronophagia in mitral cell layer of olfactory bulb eight days after inoculation. × 684.

virus as is commonly held, and that nerve roots elsewhere are equally important portals of entry, possibly indirectly by way of the blood stream to their ganglia."[5] Our own investigation shows that in experimental poliomyelitis the inflammatory reaction is not short lived and that the virus does not pass through the olfactory bulbs without producing characteristic changes. The third possibility just quoted should therefore receive careful consideration; and further studies on human material, particularly in the light of the nature of the bulb lesions in experimental poliomyelitis and the frequency of apparently unilateral involvement, should be of distinct aid in establishing the portal of entry of poliomyelitis virus in man.[7]

SUMMARY

1. The virus of poliomyelitis produces characteristic lesions in the olfactory bulbs of rhesus monkeys when it invades the central nervous system by way of the olfactory nerves.

2. These lesions are absent when the invasion of the central nervous system is by other pathways.

3. Postmortem examination of the olfactory bulbs may therefore serve to indicate the portal of entry of the virus under natural conditions.

Sixty-Sixth Street and York Avenue.

7. The authors are at present collecting a series of olfactory bulbs from cases of human poliomyelitis and would greatly appreciate the cooperation of pathologists who would send such material for study.

PLANTAR WARTS, FLAPS AND GRAFTS

VILRAY P. BLAIR, M.D.
JAMES BARRETT BROWN, M.D.
AND
L. T. BYARS, M.D.
ST. LOUIS

Foot discomfort may vary from an intermittent annoyance to a real calamity, depending on its intensity and also on the occupational and social status of the individual. A nail or a pebble inside the shoe can make normal walking next to impossible; likewise can a plantar wart or a residual hard scar if located at a bearing point. Further, prolonged use of an unnatural stance can apparently lead to secondary changes, which may be persistently annoying long after the primary cause has been removed. After successful treatment of the wart or its local sequelae, the patient may still remain crippled. An antecedent static fault has been suggested as one, or a contributing, cause, but in our limited experience the static changes appeared to be secondary rather than primary.

Plantar warts are not of rare occurrence, and their clinical behavior and therapeutic response might suggest that they are not all of similar origin. A rather common tendency to recurrence or multiplication after a surgical excision also suggests the possibility that at least some are infectious in origin. Some prove very sensitive to radium or roentgen therapy, while others of exactly similar appearance are resistant. Some disappear spontaneously, as may happen in other parts of the body or after the prolonged use of salicylic acid held in contact with adhesive plaster.

Radium or x-rays in doses well within the limits of safety is probably the best tentative plan of treatment, but excessive irradiation can be quite disastrous. Too often a patient seeking relief has for years been

Fig. 1.—A young woman in the better station of life had a plantar wart appearing seven years ago, which had been treated repeatedly with radium and x-rays. In November 1931 she presented herself for treatment for the wart from which she supposed she was still suffering. *A*, a mass of scar at the site of the original wart. For fear that some of the wart elements might still exist, this scar was removed with the cutting cautery and at a later period (April 1932) a pedicle flap with its base behind the small toe was raised from the loose sole tissue between the bearing surface of the ball and the toes. This flap was swung backward into the defect, which had been refreshened. Note in *A* the persistence of the normal skin under the ball of the great toe, while in *B* is shown a large callus, recently pared, which appeared sometime after the transfer of the flap. Since the patient lived in a distant city, it was difficult to get a satisfactory orthopedic follow up. Somewhat recently she came under the care of Dr. Ellis Jones, who, from her reports, seems to have been able to give her perfect relief by proper foot padding.

Read before the Section on Surgery, General and Abdominal, at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 15, 1936.

under treatment for a wart that had long since disappeared, the aggravated symptoms being due to pressure of a weight bearing bony point on a deeply penetrating radiation scar or a callus due to secondary static changes. If the wart has not entirely disappeared a month or six weeks after a moderate dosage of radiation, one of two plans should be followed: One plan is knife excision and immediate suture; the other

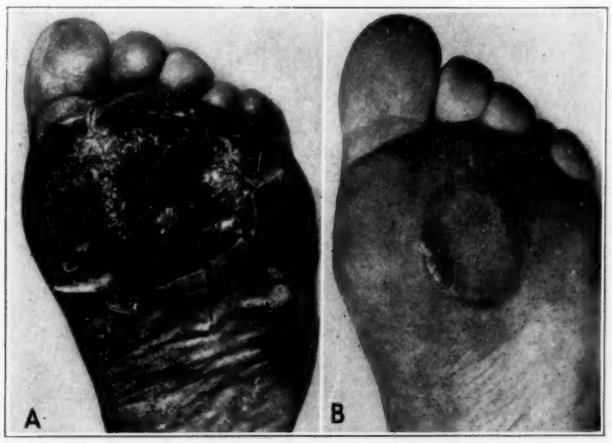

Fig. 2.—The foot of a very heavy professional man, who had been almost totally incapacitated because of a plantar wart on the middle of the ball of the foot. It was treated with x-rays. *A*, an acute dermatitis which appeared some weeks after the patient had gone to a seashore resort. For some rather inexplicable reason, a wide surgical removal of the damaged area was made in the acute stage of the inflammation. The destruction of the fat pad down to the bone left the man almost unable to walk. *B*, correction by the transplantation of a pedicle flap of skin and fat from the calf of the right leg. This has given a comfortable bearing pad, but the skin has been slow to respond to environmental change and for a long time he wore adhesive plaster for its protection.

is accurately limited actual cautery destruction. The latter is simple and effective and, if the wart is not large, is ordinarily neither long confining nor followed by a painful scar, provided the surrounding skin and underlying fat have been spared. This has been our procedure of choice.

A reaction from excessive irradiation may result from oversensitivity of the individual, overdosage, or both, but ordinarily it will not have been pushed beyond production of a dermatitis. This, although painful, will usually, if not further irritated, subside spontaneously, possibly leaving a small area that will require but relatively simple surgical repair. The most crippling results have come from ill advised treatment of a postirradiation disturbance. Here, as elsewhere, acute radium or x-ray burns are decidedly intolerant of a wide range of chemical applications. Among these is bromine, which is an ingredient of certain analgesic applications that have proved to be quite soothing in various other conditions, but here its use has been followed by great aggravation, even causing massive slough of the inflamed area. Another unfortunate procedure is the early removal of the skin and fat pad from the inflamed irradiated area. Under these circumstances patients have suffered for years before the necessity for an extensive repair has been recognized.

A distressing "cornlike" scar that may follow the primary wart destruction should be completely excised, and if the defect is small it can be closed by skin suture, perhaps with some drawing together or switching of the fat pad. For larger defects that cannot be corrected by these simpler plans, a pedicle flap which includes skin and part thickness of the pad can be switched from a non-weight bearing surface of the sole, either of the front of the ball just behind the toes or of the inner half of the central part, and the resulting defect is immediately covered by a skin graft. If the skin alone is missing but with sufficient fat pad persisting, this can be covered with a thick split graft. Even when there has been a very large loss of both skin and pad, as occurs from fire burns, or accidents caused by the automobile or machinery, a split skin graft placed directly on the muscles or granulations will effect immediate coverage, and the subsequent use of a fine meshed sponge rubber insole will serve as a partial, but more or less practical, substitute for the lost fat pad. In the few instances in which I have transferred a fat-skin flap from the calf of the other leg to the bearing surface of the sole, the result has proved somewhat disappointing. The leg fat lacks the tough resilience of the normal sole pad, and the epithelium of the transplanted skin itself fails to harden to its new task. In one case I achieved my end by constantly protecting the transplanted skin with adhesive plaster. In another, a quite satisfactory final result was obtained by excising two persistent "trophic" ulcers, and immediate split skin grafting to the underlying scarred fat of the transplanted leg flap. Because of the resistant "bearing" surface that develops on the outer dorsal surface of an uncorrected "clubfoot," I have sought to transfer large pedicle flaps from this area but have encountered real difficulty in preserving the circulation even after delaying the transfer of the flaps.

The crippling or painful calluses that are apt to develop and stubbornly persist in some other area of plantar skin after a localized wart has been controlled may prove most embarrassing. I am beginning to be a little uncertain as to two points in their regard: the first is whether the persistence of the callus is entirely due to an acquired faulty position of the foot; the

Fig. 3.—The foot of a man who for some years had suffered from the painful scar of a cured wart. The small actual destruction of the foot pad was compensated for by undermining and shifting neighboring tissue, and the coverage was made with a split skin graft. This gave a very satisfactory result.

second, whether the conservatism that I have habitually exercised in the past has all been to the patient's best interest, the possibly fantastic doubt having arisen as to whether the tendency to callus growth can always be eliminated by partly relieving the pressure on that spot. My belief is that in every case of crippling callus the

patient should be given the benefit of the most skilful orthopedic treatment available; but if these hangover cases do not get relief by corrective shoeing within a reasonable time, I can at present see no reason for not eliminating the callous spot by excision and immediate switching of a fat-bearing plantar flap, a plan that has proved most successful in the treatment of certain painful plantar scars.

Grand Avenue and Olive Street.

Fig. 4.—The transplantation of a leg flap under the ball of the foot and the heel to replace scars from a deep burn. Note three trophic ulcers, which subsequently developed with use and which were extremely persistent. The foot was finally made well and useful by removing these ulcers, including border and base down to the soft scar in the underlying fat pad and applying split skin grafts.

ABSTRACT OF DISCUSSION

DR. ELLIS FISCHEL, St. Louis: Irradiation is the accepted method of treatment. As the authors have emphasized, the first consideration in using radiation is not to do damage. My experience has been limited to the use of radium in the following manner: 50 mg. of radium element contained in 12.5 mg. steel alloy needles, placed within a 1 mm. brass or silver capsule, and around that approximately a millimeter of rubber. Then a fenestra is made through a millimeter of lead and the bottom of that fenestra covered with a millimeter of rubber. The fenestra is just large enough to contain the wart. One treatment of two hours' duration with this applicator has usually been sufficient, and in even those cases previously treated by x-rays a dangerous reaction has never been observed. Of twenty-eight private cases treated in this manner, twenty-one responded favorably to one treatment. But one must not be in too much of a hurry. The average patient may be expected to have relief from pain in approximately three or four days, but the wart does not disappear until sometime later, usually in about two weeks. However, occasionally a patient will go four weeks before stating that he no longer notices the wart. I wait four weeks. If the wart is still present after four weeks' time the dose is repeated. Of the twenty-eight cases it is known that fifteen had satisfactory results. There were satisfactory immediate results in ten additional cases but there has been no long follow up. Plantar warts may occur in a callous area. I do not know whether it is the callus or the wart that is causing the pain. By taking a stiff blunt probe and pressing on the black wart and then around the wart on the callus, one can easily obtain differentiation. If pressure outside the wart causes pain, one must realize that the callus may have a good deal to do with it; then one must differentiate between the pain from the callus and the pain from a possible underlying periostitis. The latter is the bugbear of all this treatment, because patients who have a periostitis from long pressure over the head of the metatarsal bone are not going to be cured by any method of local treatment of the skin condition. The molehill has now become the mountain, the proper handling of which has been so ably presented by Dr. Blair and his co-workers.

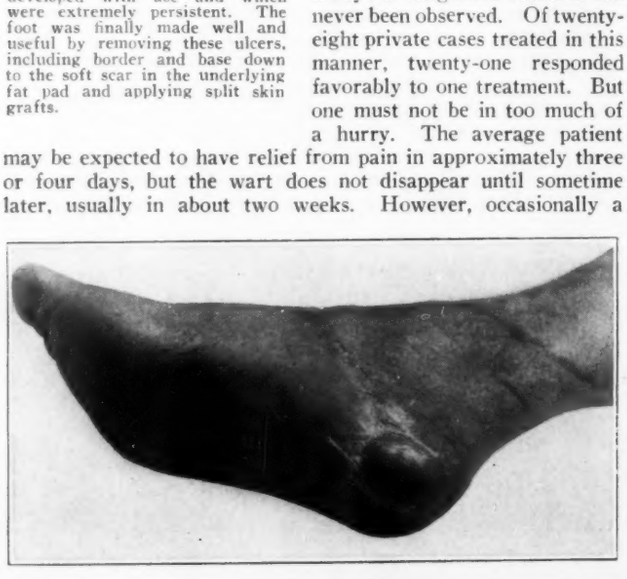

Fig. 5.—A deep loss on the outer and under surface of the heel. To remedy this an attempt was made to prepare a delayed flap from a non-bearing part of the foot. This was not used because of impaired circulation. The scar covering the original defect was replaced by a split skin graft, and a sponge rubber pad has made a very satisfactory substitute for this partially lost fat pad.

DR. JOSEPH J. ELLER, New York: I agree with the authors that only safe doses of radiation should be used on account of the sequelae which may occur from more destructive measures. With the dosage of from 80 to 100 milligram hours of gamma radiation to the square centimeter of tissue, plantar warts should undergo involution. Plantar warts are not true new growths. They are due to an infectious virus. From 60 to 70 per cent of these lesions will disappear on irradiation with radium or roentgen rays. Many dermatologists in this country now treat plantar warts by means of 2,500 and 2,800 roentgens unfiltered. In other words, they use the warty excrescence as a filter, and with that dosage used in one treatment, a good many of the lesions will disappear. If they do not disappear, there is a problem. I have found that whenever surgical measures are used following irradiation of skin tissue a keloidal scar results, and while the wart may be removed either by excision or by electrocoagulation, a keloidal scar formed as a secondary growth is just as painful as the original wart. The patient and the physician frequently think erroneously that there has been a recurrence. One has to resort to small safe filtered doses of radiation to dissolve that keloid. Excising a keloid does not make it disappear. It only results in a larger one. I agree with the authors that the only treatment for post-irradiation injury is excision, care being taken to preserve the fat pad; later, to counteract any hypertrophic scar, small doses of radiation should be given. Another thing which dermatolo-

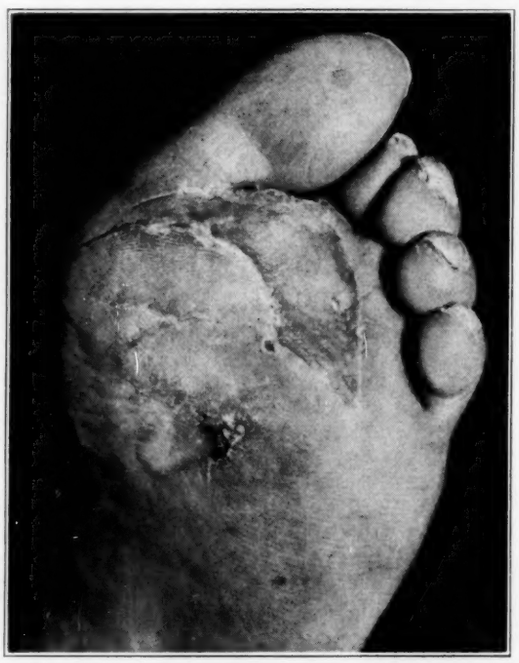

Fig. 6.—The foot of a working man with an alcoholic neuritis and anesthesia which accounted for his standing on the floor of a partially cooled furnace long enough to burn his feet. This caused wide destruction of the skin and pad in the balls of both feet. On the foot shown, repair was made by shifting a fairly large flap from behind the toes to beneath the heads of the metatarsal bones. The resulting defect from the switching of the flap was covered with a split skin graft. On the left foot the destruction was much more extensive. The bare area was covered with a split skin graft placed on the plantar fascia, and a sponge rubber pad was used.

gists have observed is that plantar warts, when destroyed by electrocoagulation, frequently result in very small slow-healing ulcers. With this therapy one must not promise that the patients can get back on their feet in less than three weeks. There is very little that one can do to hurry the healing. Perhaps in these cases after destruction the best treatment would be an immediate plastic repair, without waiting for slow granulation and healing, which sometimes takes even as long as six weeks.

DR. VILRAY PAPIN BLAIR, St. Louis: Dr. Eller brought out the necessity of giving orthopedic care of the foot after the wart has been cured. There is little I know less about than scars, but I do think I know this much, that anything that will put lateral tension on the wound will tend to make a bad scar. If the loss is limited to the skin, a skin graft will suffice. If the defect is too large to permit the sliding in of a bordering fat pad, the switching of a pedicle flap of skin and fat pad will probably be the safest plan. When heat destruction is indicated, I use a fine platinum, electrically heated, cautery point. In a much treated case, knife removal will probably be the better, as it is likely that the wart is already cured and the flap can be switched in place at the same sitting.

ULCERATIVE LESIONS OF THE SKIN IN LYMPHOGRANULOMA INGUINALE

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AND
MINNIE OBOLER PERLSTEIN, M.D.
CHICAGO

Ulceration of the skin as a part of the syndrome of lymphogranuloma inguinale has not received much notice in the discussion of the clinical manifestations of this disease.

Huguier [1] in 1848 described esthiomene as a chronic hypertrophy and ulceration of the vulva which may be associated with similar involvement of the vulvo-anal area, rectal ulceration or stricture. In the majority of his cases there was also infiltration of the inguinal lymph glands. He subdivided his entity into four main clinical groups: a hypertrophic vegetative type, an elephantiasic type, a type characterized by the formation of fistulas, and an ulcerative type.

Fournier [2] in 1873 described the occurrence of a syndrome of indolent edema of the vulva which was frequently associated with inguinal lymphopathy. He believed that it was syphilitic in origin but distinct from his "syphilome anorectale." Ulceration of the vulva is not mentioned in his description.

In 1896 Koch [3] reported twenty cases, all of which presented a syndrome which he designated as "ulcus vulvae chronicum elephantiasicum." All these patients had associated pathologic conditions of the inguinal lymph glands. He summarized the symptomatology as follows: [4]

> The labia majora were the seat of more or less marked thickening, with ulceration, . . . rather less commonly the labia minora and clitoris were affected, . . . the skin had a bluish red color and was ulcerated; sometimes . . . the mons, the commissure and perianal region were involved in the infiltrative process. . . . Ulceration might occur in any part of these infiltrated tissues but was most common at the commissure, the opening of the urethra, on the inner surface of labia minora and clitoris. The ulcers in shape were often irregular or dentated; with a yellowish shiny base, callous thickened steep sides, with sometimes undermined edges, and showed as a rule no tendency to epitheliation, though sometimes healing on one side and extension on another was noted. Perforation of the nymphae, fourchette, or urethrovaginal and rectovaginal walls might occur, with the formation of fistulae; or there might be greater destruction of tissues, with the production of a cloaca, limited by portions of infiltrated skin and mucous membrane; rectovesical fistula might also be produced. The rectum might be severely involved, the mucous membrane of the anal canal altered to form a rigid ulcerated tube, with an ulcerated anal opening, sometimes also the seat of papillomata and extroversion. In some cases a rectal stricture was also present.

Koch believed that this condition was not due to syphilis, tuberculosis or ulcus molle and had no suggestions to offer concerning its etiology.

Taussig [5] in 1922 named the condition hypertrophic ulcerative chronic vulvitis of undetermined etiology.

Jersild [6] in 1920 was impressed by the frequency of the coexistence of elephantiasis vulvae and rectal stricture and named this clinical association the genito-anorectal syndrome.

Following the advent of the Frei test,[7] Frei and Koppel [8] in 1928 established their cases of genito-anorectal syndrome as lymphogranuloma inguinale (Durand, Nicolas and Favre [9]).

In a series of 500 patients with lymphogranuloma inguinale, we have observed twelve cases of ulceration. We present the detailed clinical reports of three of these patients together with bacteriologic and histologic studies. These three cases illustrate the types of clinical ulceration that may occur in lymphogranuloma inguinale:

1. Ulceration of the skin only—lymphitis (case 1).
2. Ulceration of the skin secondary to a previous lymph gland involvement (case 2).
3. Ulceration developing on an existing esthiomene (case 3).

REPORT OF CASES

CASE 1.—*History.*—A Negress, aged 40, gave a history of rectal pain and itching associated with constipation of twenty-three years' duration. Eight years before her admission to the hospital a rectal operation was performed, since which time she has had pencil-sized stools and a purulent rectal discharge. During the preceding five months she had pruritus vulvae associated with pain and burning on urination. Her general health had been good. Her husband was well and had no similar complaint. Physical examination was essentially negative except for the genital pathologic condition (fig. 1). The perineal tissues were of firm cartilaginous consistency with induration of the perianal and adjacent crural areas. There was a fissure extending from the vagina to within 1 cm. of the anus, almost forming a cloaca. On the inner surface of both labia minora was a superficial ulceration which extended on to the vaginal mucosa and adjacent perineum. The margins of the ulceration were serrated and soft. The base of the ulcer

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Read before the Section on Dermatology and Syphilology at the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 15, 1936.

From the Department of Dermatology, University of Illinois College of Medicine, service of Dr. F. E. Senear, and the Dermatological Service of the Cook County Hospital.

1. Huguier, P. C.: Mémoire sur l'esthiomène ou darte rongeante de la region vulvo-anal, Mém. de l'acad. de méd. 1848, reprint Paris, 1849.
2. Fournier, A.: Leçons sur la syphilis, 1873.
3. Koch, F.: Ulcus Vulvae chronicum elephantiasicum, Arch. f. Dermat. u. Syph. **34**: 205, 1896.
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6. Jersild, O.: Pathogeny of So-Called Syphilome Anorectal, Ann. dermat. et syph. **1**: 62, 1920.
7. Frei, Wilhelm: Eine neue Hautreaktion bei Lymphogranuloma inguinale, Klin. Wchnschr. **45**: 2148 (Nov. 5) 1925.
8. Frei, Wilhelm, and Koppel, Alice: Ulcus Vulvae chronicum elephantiasicum (Esthiomene) und sogenanntes Syphilome anorectal als Folgeerscheinungen der Lymphogranulomatosis inguinales, Klin. Wchnschr. **7**: 2331 (Dec. 2) 1928.
9. Durand, M.; Nicolas, Joseph, and Favre, M.: Lymphogranulomatose inguinale: Subaigue d'origine génital probable, peut-être vénérienne, Bull. et mém. Soc. méd. d. hôp. de Paris **35**: 274, 1913.

was bright red, smooth and painful. There were no nodules on the base and there was little bleeding on trauma. The rectal mucosa was nodular and there was a rectal stricture about 3 cm. from the anal orifice.

The Frei test was positive; the dmelcos, blood Wassermann and Kahn tests were negative. Darkfield examination was negative.

Bacteriologic examinations revealed many bacilli and cocci but no Donovan bodies or Ducrey bacilli.

Histologic Examination.[10]—The specimen consisted of a small piece of skin with an irregular ulcer. The floor of the ulcer was formed by a very cellular granulation tissue, which was composed of round cells and polymorphonuclear leukocytes and of capillaries with prominent endothelial cells. Plasma cells were numerous, and dense infiltrations extended beyond the ulcer into the papillary and subpapillary layer, which was covered by an intact epithelium. The rete pegs were elongated and in the basal portions became widened and enclosed hyalinized epithelial cells. In many places polymorphonuclear leukocytes invaded the rete pegs.

Fig. 1.—Ulceration of the inner surface of the labia minora.

CASE 2.—*History.*—A Negress, aged 20, was seen in June 1935 with the following history: One year previously she had a painful "blister" on the vulva, which slowly enlarged. Four weeks after the appearance of the vulvar lesion the right inguinal area became swollen and painful; later the left inguinal area became involved. The lymphatic glands drained spontaneously and large ulcers developed in the right inguinal area. Her general health had been good. The essential pathologic changes on examination were limited to the genital area (fig. 2). The right inguinal area was the site of two quarter-sized (24 mm.) superficial necrotic painful ulcers with a similar, larger lesion in the left inguinal region. The labia were markedly endematous. These ulcers were clinically identical, having sharp margins, rolled edges and a clean hemorrhagic base. Adjacent to the ulcer on the right inguinal area were two puckered, scarred bands.

The Frei test was positive, the Ito-Reinstierna reaction was negative, smears from the vulvar ulcer were negative for gonococci, and the blood Wassermann reaction was positive. Bacteriologic examinations were negative for Donovan bodies, Ducrey bacilli and tubercle bacilli.

Histologic Examination.—The specimen taken from the ulcer in the inguinal region showed a small piece of skin with a moderate acanthosis of the epidermis. The papillary layer of the cutis was infiltrated by lymphocytes and plasma cells and the infiltrations followed the capillary blood vessels into the subpapillary layer. In this region the infiltrations became more extensive and had the tendency to fuse together. Between the lymphocytes there were swollen histiocytes and plasma cells, and the adventitial cells of adjacent capillaries often joined with one another to form a loose cellular reticulum. In the reticular zone of the cutis the infiltrations again broke up into perivascular round cell accumulations similar to the picture seen in the papillary layer.

10. The histologic examinations mentioned throughout this article were done by Dr. R. H. Jaffé of the Cook County Hospital.

Treatment consisted in the intradermal injections of Frei antigen[11] every three days for a period of three weeks. The ulcers in the inguinal areas involuted completely, and the vulvar ulcer was almost healed at the end of this time. Antisyphilitic treatment was then instituted. There was complete healing of all ulcers by September 1935.

CASE 3.—*History.*—A Negress, aged 32, was first seen in March 1935. In 1932 a painful nodule appeared on the right vulva three weeks after intercourse. The nodule ulcerated and was associated with a swelling of the labia. The right inguinal region subsequently became swollen and tender and the gland ruptured spontaneously and drained slightly for about one year.

There was bilateral shotty inguinal adenopathy. The vulva was hypertrophic. Between the labium majus and minus was a crater-like ulcer 2 cm. wide and 1 cm. deep with red and granular walls. The base was yellowish gray with a moderate yellowish exudate (fig. 3).

The Frei test was positive; the dmelcos, blood Wassermann and Kahn tests were negative. Darkfield examination was negative.

Bacteriologic examinations revealed many bacilli and cocci but no Donovan bodies or Ducrey bacilli.

Histologic Examination.—The specimen consisted of a small piece of skin with an ulcerated area, in the region of which the epidermis was missing. The floor of this ulcer consisted of a granulation tissue which originated from the subpapillary layer of the cutis and was very cellular. It contained thick-walled capillary blood vessels at regular intervals and between and about these blood vessels were dense accumulations of small and medium sized round cells with scanty cytoplasm. Between the lymphatic cells were found a few plasma cells and polymorphonuclear leukocytes, and near the free surface of the ulcer the leukocytes became more abundant. The capillaries had swollen endothelial cells, and attached to the outer aspect were adventitial cells which were prominent and extended between the adjacent round cells. The infiltration was sharply circumscribed and in the surrounding cutis loose accumulations of lymphocytes and histiocytes were seen which were scattered between the connective tissue bundles or centered about small blood vessels.

Fig. 2.—Ulceration of the skin on a preexisting suppurating inguinal lymphadenopathy.

BACTERIOLOGY[12]

The bacteriologic flora from nine cases of lymphogranuloma inguinale and one of granuloma inguinale was investigated. The surface of the lesions was well washed with sterile saline solution, sterile gauze sponges

11. Wien, M. S., and Perlstein, Minnie O.: The Intradermal Treatment of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **28**: 42 (July) 1933; Brit. J. Dermat. & Syph., to be published.

12. The bacteriologic examinations were made by Dr. Virginia Fisher of the Department of Bacteriology, University of Illinois College of Medicine, Dr. L. L. Arnold, director.

being used. Direct smears were studied by means of the Gram stain, and darkfield examinations were made. A small piece of tissue was curetted from the lesions and emulsified in a small amount of sterile saline solution. This material was then used for the inoculation of the following mediums: plain agar, blood agar, honey agar, Endo agar, semisolid dextrose agar and brain broth. These were incubated at 37.5 C. for from twenty-four to forty-eight hours and the organisms studied by smears and additional cultural methods.

Organisms Found on Bacteriologic Examinations *

Case Number	Spirochetes	B. Ducreyi	B. Coli	Staphylococci	Hemolytic Streptococci	Yeasts	Streptothrix	Sarcinae	Diphtheroids	Bacilli of Fusiform Type	Large Gram-Bacilli (Spores)	Pleo Gram Bacilli
1	0	—	+	—	+	—	+	—	+	—	—	—
2	0	—	—	+	+	—	—	—	+	+	—	—
2	0	—	—	+	+	—	—	—	+	+	—	+
2	—	—	—	+	+	—	—	—	+	+	+	+
3	0	—	—	+	+	—	—	—	—	—	+	—
3	—	—	+	+	+	+	+	+	+	+	—	+
3	—	—	—	+	+	—	—	—	+	+	—	+
4	0	—	—	+	+	—	+	+	—	+	+	—
5	0	—	—	—	+	—	—	—	—	+	+	—
5	0	—	—	+	+	—	—	+	—	+	—	+
6	0	—	—	+	+	—	—	+	—	+	—	—
7	—	—	—	+	+	—	—	—	+	—	+	+
8	T. refringens (dead)	—	—	+	+	—	—	—	+	+	+	+
9	T. refringens	—	—	+	+	—	—	—	—	—	+	+

* 0 indicates no examination made; — not found; + organisms found.

The most regularly occurring organisms are shown in the accompanying table. It should be observed that no Spirochaeta pallida and no Ducrey bacilli were found in any of the lesions; also that in spite of the location of the lesions in the inguinal, vaginal and anal regions, B. coli appeared very rarely. Both Staphylococcus albus and aureus were found; the streptococci were usually of the hemolytic variety.

Organisms other than those shown in the table were found in some specimens but with no regularity.

It seems reasonable to conclude that the organisms found are most probably secondary invaders which may usually be found in necrotic lesions.

DIFFERENTIAL DIAGNOSIS

The ulcerative lesions occurring in lymphogranuloma inguinale are superficial in character, irregular in outline and variable in size and contour. The normal skin may merge abruptly with the ulcer or form a thin overlapping cordlike band with a tendency to serration. The walls of the ulcer are usually of a shallow, shelving type. The base of the ulcer is vivid red, shining, and of a smooth velvety texture. There is an absence of verrucous nodules or granulations in the base or margins of the ulcer. A thin, clear mucoid secretion may cover the lesion. In neglected cases this may assume a purulent character. The ulcer spreads by peripheral extension, is not auto-inoculable and shows no tendency to spontaneous healing. The lesions are painful on palpation. The Frei test is positive. Histologic examination reveals a nonspecific microscopic picture of tissue suppuration with ulceration of the skin and a predominance of plasma cells in the infiltrate. No organisms are seen in the stained sections.

This condition must be differentiated from those entities associated with superficial ulceration of the cutaneous surface. Chief among these are chronic chancroidal infection, granuloma inguinale, ulcerative tertiary syphilis, tuberculosis cutis, gonorrhea, ulcus vulvae acutum (Lipschütz), ulcus vulvae simplex chronicum, traumatic ulcer and epithelioma.

Chronic chancroidal infection is a contagious and auto-inoculable ulceration caused by the streptobacillus of Ducrey. The lesions are usually multiple, painful, dime-sized (18 mm.) ulcerations that have perpendicular undermined edges, a dirty yellow base and a foul smelling discharge. The associated inguinal adenitis or bubo is a unilobular lesion which drains a thin foul smelling pus containing the Ducrey bacillus. The dmelcos and Ito-Reinstierna reactions are positive.

Granuloma inguinale is a superficial ulceration of the skin produced by Donovan bodies.[13] The ulcers are contagious and auto-inoculable and present numerous shiny verrucous vegetating nodules of granulation tissue at the margins and dispersed throughout the base of the ulcer. This ulceration after healing produces a dense white contracting scar tissue. The process is painless and, as a rule, unaccompanied by adenopathy.

Ulcerative tertiary syphilis results from the coalescence of groups of discrete "punched out" ulcers that tend to assume an arciform or annular configuration and heal spontaneously, producing a thin white atrophic scar with hyperpigmentad borders. The serologic reaction of the blood is positive and the condition involutes with antisyphilitic treatment.

Tuberculosis cutis of the ulcerative or gummatous variety presents irregular painful ulcers and fistulas, the base of which is uneven and covered with yellowish granulation tissue. Smears of the discharge or stained histologic sections reveal the tubercle bacilli. The histologic picture reveals a tuberculous architecture.

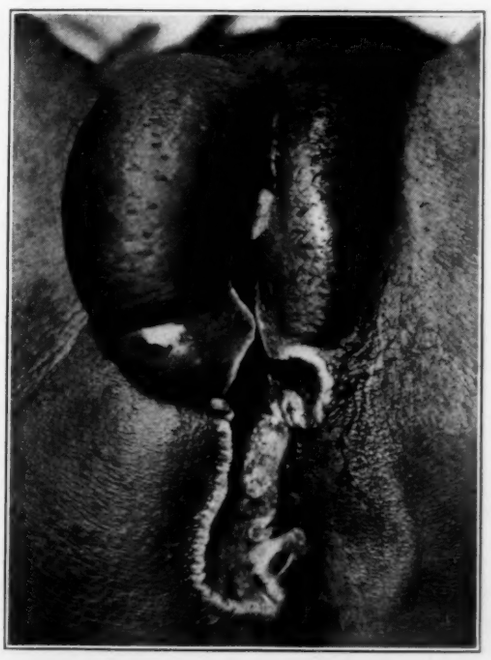

Fig. 3.—Ulceration developing on existing esthiomene.

Ulcus vulvae acutum (Lipschütz[14]) is a painful recurrent ulceration of the external genitalia. The

13. Donovan, C.: Indian M. Gaz. **40**: 414, 1905.
14. Lipschütz, Benjamin: Ueber eine eigenartige Geschwursform (Ulcus vulvae acutum), Arch. f. Dermat. u. Syph. **114**: 363, 1913. Wien, M. S., and Perlstein, Minnie O.: Ulcus Vulvae Acutum Associated with Lesions of the Mouth, J. A. M. A. **98**: 461 (Feb. 6) 1932.

ulcers are superficial, painful and not auto-inoculable and they heal spontaneously. B. crassus is usually present in the ulcers.

Ulcus vulvae simplex chronicum[15] occurs in old prostitutes and affects the fourchette. It has no tendency to spread and is not associated with inguinal adenopathy, hypertrophy of the vulva or stricture of the rectum. The Frei and dmelcos tests are negative.

Gonorrheal infection may produce a vulvitis associated with erosive lesions, the margins of which may be variable and the base a dusky red and with a granular surface. Smears are positive for gonococci.

Traumatic ulcers have a characteristic, irregular or fissured form with a preceding history of injury. The lesions heal with marked rapidity.

Epithelioma in the genitocrural region is characterized by the occurrence of a granulomatous new growth in which the ulceration occurs as a secondary phenomenon. The lesion is slow in growing, often with rolled pearly margins, and the nodules are friable and bleed freely. Histologic examination reveals the characteristic changes of a malignant condition.

COMMENT

Chevallier and Bernard[16] studied the histologic aspects of lymphogranuloma inguinale and concluded that the classic poradenitis is due to the association of two processes, an adenopathic and a cutaneous. The adenopathic phase consists of a number of gummas separated from the upper hypoderm by a band of healthy tissue. The progression of these gummas toward the surface of the skin can be seen in some sections. The cutaneous phase involves the upper part of the hypoderm and is accompanied by lymphangitis. At times the cutaneous ulceration develops before the deep gummas have reached the skin. These writers believe that there may logically exist either a pure cutaneous or a pure lymph gland form in addition to the classic forms of combined lymph gland and skin involvement. The reports in the literature make little mention of the ulcerative phase (cutaneous form) of this complex syndrome.

The cases reported demonstrate the three types of clinical ulceration that may occur in lymphogranuloma inguinale and illustrate the histologic aspects mentioned by Chevallier and Bernard.

The cutaneous phase (lymphitis) is clinically and histologically demonstrated by case 1. This type of involvement is analogous to that previously reported, among others, by Wien, Perlstein and Neiman,[17] and by Pinard and Fiehrer[18] as occurring in nodular form with the formation of secondary ulcerative plaques in the skin. In this instance the epidermal lymphatics and those of the upper part of the hypoderm are affected with the virus of lymphogranuloma inguinale, and an inflammation results that manifests itself as a superficial ulceration of the skin.

The occurrence of ulceration of the skin secondary to involvement of the underlying lymph glands — the adenopathic phase—is demonstrated by case 2. Similar lesions may occur in males, as reported by Midana.[19] We have seen two men who presented inguinal adenopathy associated with superficial ulceration of the abdomen and inguinal regions.

The occurrence of chronic hypertrophy and ulceration of the vulva (esthiomene-Huguier[1]) is demonstrated by case 3. This case is a classic example of the entity first described by Huguier and may be associated with rectal stricture giving rise to the genito-anorectal syndrome of Jersild.

SUMMARY

1. Twelve cases of ulceration of the skin occurring in our series of 500 cases of lymphogranuloma inguinale were observed and are reported with clinical, bacteriologic and histologic records of three cases. Two men presented ulceration of the skin in association with inguinal adenitis.

2. Three types of ulceration of the skin are demonstrated by the cases described:

(*a*) Ulceration of the skin only.

(*b*) Ulceration of the skin secondary to an existing lymph gland involvement.

(*c*) Ulceration developing on an esthiomene.

3. The bacteriologic flora of the ulcerations was thoroughly investigated. The organisms found were probably secondary invaders.

4. Histologic examinations of the ulcerations were nonspecific. There was a uniform picture of ulceration, fibrosis and plasma cellular infiltration.

5. We feel that cases of superficial ulceration in the skin, resistant to the ordinary or specific methods of therapy, especially when occurring in the genitocrural area, should be tested with Frei antigen, diagnostically and therapeutically, in order to rule out the possible relation of the ulceration to lymphogranuloma inguinale.

104 South Michigan Avenue — 30 North Michigan Avenue.

ABSTRACT OF DISCUSSION

DR. C. C. TOMLINSON, Omaha: I find it difficult to accept the fact that the cutaneous ulcerative phase may exist independent of underlying suppurative lymphadenitis. Is is not possible that a few small nodes in the rectovaginal septum, the anorectal nodes of Gerota, or other lower pelvic nodes may be draining through small fistulas which cannot be detected on examination and which are responsible for the persistent cutaneous destruction, such as is exemplified in their case 1, and which they describe as lymphitis? Case 2 is portrayed by the authors as cutaneous ulceration secondary to underlying inguinal lymphadenitis. With reference to case 3 I would like to ask if it would not be possible, or even probable, that there existed an underlying suppurative process in the lymph nodes of the rectovaginal septum which was responsible for the granulomatous vulvitis referred to as esthiomene with ulceration. Although I do see the genito-anorectal syndrome occasionally in Omaha, I have not encountered persistent cutaneous ulceration as described by the authors. The chronic cases for the most part have presented as rectal stricture, perineal sinuses or esthiomene. We have difficulty in following individual cases for long. We do not have facilities for prolonged hospital observation, and the majority of our colored patients leave us when we exhibit what to them may seem undue interest in their condition. We have instituted intradermal Frei antigen treatment in several women with rectal stricture as a preoperative measure (previous operations having failed to cure their stricture) but have not been able to hold these patients long enough to evaluate the therapy. I believe that in our early cases filtered x-ray therapy over the involved lymph nodes

15. Jacobsen, R., and Pardo Castelló, V.: Ulcus Vulvae simplex chronicum, Acta dermat.-venereol. **16:** 133 (July) 1935.

16. Chevallier, Paul, and Bernard, J.: Forme cutanée pure de la maladie de Nicolas-Favre, Bull. Soc. franç. de dermat. et syph. **39:** 1351 (Nov.) 1932.

17. Wien, M. S.; Perlstein, Minnie O., and Neiman, B. H.: Inguinal Lymphogranuloma in Its Relation to Stricture of the Rectum. Arch. Path. **19:** 331 (March) 1935.

18. Pinard, Marcel, and Fiehrer, Albert: Forme cutanée de la maladie de Nicolas-Favre: Reactivatun d'une intradermo-réaction de Frei ou réaction rétardée, Bull. Soc. franç. de dermat. et syph. **39:** 1630 (Dec.) 1932.

19. Midana, A.: Cutaneous Lesions in Acute Inguinal Lymphogranulomatosis of Nicolas and Favre, Gior. ital. di dermat. e sif. **75:** 1743 (Oct.) 1934.

has been of value and that intradermal Frei antigen treatment is also decidedly advantageous. At times it is difficult to find satisfactory early cases from which to make sufficient antigen to treat other patients. It is our intention to make virus culture antigen (J. T. Tamura, THE JOURNAL, Aug. 11, 1934, p. 408) in larger quantities than one can hope to obtain with pus-derived antigen, and to treat a series of cases with it.

DR. HARRY M. ROBINSON, Baltimore: May I sound a warning about the positive Frei test. It means past or present lymphogranuloma inguinale, but not every lesion that gives a positive Frei test is lymphopathia venerea. Even though a patient has a positive Frei test and a fluctuant bubo, the resultant pus is not accepted as a good antigen until it has been tested with known cases. In our groups of cases, my associates and I differ from the authors in that with a large Negro clinic we have found 1 per cent positive Frei tests in white persons and 60 per cent in Negroes (all of whom had syphilis).

DR. SAMUEL GOLDBLATT, Cincinnati: When multiple Frei antigens are used, one is likely to receive varying results on the same individual. We in Cincinnati have a habit of testing at the time for diagnosis with about fifteen different antigens. These are controlled by old tuberculin and bovine tuberculin. The antigens, most of which are made in the clinic from known cases, are also controlled by monkey brain antigen, which I obtained from Dr. Hellerström of Stockholm. It is not unusual to see varying degrees of positiveness with the first four or five antigens, one being four plus, two three plus, three one plus, four negative. In case 2, with clinically the same type of results, antigen 1 may be negative and antigen 5 positive and the others varying. In case 4 the antigens that previously varied may give the same result. I am at a loss to understand this phenomenon; I am simply reporting it as an observation. I can also confirm the fact that in colored patients 60 per cent positive Frei reactions are obtained as a routine. In a mixed group, almost equally white and colored in the Cincinnati workhouse, about 50 per cent of Frei tested groups report positive. It is not always possible in positive Frei reported cases to find evidence or history of the infection. Dr. Wien will probably remember a case which I presented at the last Cincinnati session of the Mississippi Valley and Central States Dermatological Society, a woman of about 50 who had a tremendous elephantiasis with sinuses involving the entire vulva and the right buttock. In this case all the Frei antigens had been repeatedly negative, although six years previously the woman had had clinically a definite papular syphilid; her Wassermann reaction at that time and on all repeated occasions had also remained negative. Tested with material taken from her own glands, the patient was negative. We have surgically excised with the electrocautery this entire area in two stages; the last stage, that of the buttock, is at present healing. We were never able to find a definite rectal stricture, although she has had very long attacks of serious diarrhea which may be a precursor of the stricture.

DR. PAUL A. O'LEARY, Rochester, Minn.: My experience has been quite the opposite of Dr. Robinson's in that all my cases of lymphogranuloma inguinale have been in white persons. Drs. Wien and Perlstein have furnished me with the diagnostic antigen, which has also been highly efficient therapeutically in our patients when the treatment was started early in the bubo stage. I wish to stress the point that we now have evidence that lymphogranuloma inguinale is a systemic disease and not solely a genital infection. In support of this contention the following complications may be cited: Cutaneous ulcerations of lymphogranuloma inguinale have been reported occurring elsewhere than about the genitalia; likewise I have seen on two occasions a follicular reaction on the skin, of the nature of an "id," in patients with acute signs of the disease. In addition to rectal stricture, the retroperitoneal lymph glands may become involved in the early cases and produce difficult differential diagnostic problems. Perhaps the authors could give some figures on the relative incidence of chancre, chancroid and the early lesions of lymphogranuloma inguinale. I ask this question because patients with a chancroid are now seldom seen in our clinic.

DR. ANDREW L. GLAZE, Birmingham, Ala.: A case of lymphopathia venerea in a petty officer of the navy, retired, was observed this spring. Chronic superficial ulcerated lesions of the skin of four years' duration were present. The scrotum was involved. Much of the skin of the glans penis was destroyed. Frei tests were done with different antigens, mouse brain and antigens from human sources; all were strongly positive. The histologic picture was consistent with the disease in question. Bacteriologic and serologic studies as well as therapeutic tests aided in ruling out other possible disorders.

DR. MARION B. SULZBERGER, New York: Because the old name of lymphogranuloma inguinale had led to confusion with lymphogranuloma on the one hand and with granuloma inguinale on the other, Dr. Wolf and I thought it would be better to call this disease by some other name. And so in 1932 we suggested the name of lymphopathia venerea (Lymphopathia Venerea, *Brit. J. Dermat. & Syph.* **44**:192 [April] 1932). I was fortunate enough to be able to perform the first Frei tests in the United States, using Frei "antigen" which I had brought with me from Europe. After performing this test, which I had learned from Prof. Walter Frei in Breslau, Dr. Wolf and I in 1931 reported the first positive tests on patients in New York and submitted this report to THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. THE JOURNAL sent back this brief report with the statement that the disease and test discussed in our communication were not of sufficient interest to the general medical profession to warrant its publication in its pages. I recount this fact merely to show how rapidly the American medical public has learned about this disease; for my story shows that both the disease and the test were unrecognized here only a few years ago (1931) and I think that we need not emphasize how much real interest has since been aroused in this country by the Frei test and by the possible unification of all these different manifestations, by means of its employment. The interesting point is that daily new manifestations are being found which can be regarded as probably due to this infection. I should like to mention here two possible further additions: One is colitis, as probably simply due to this virus, occurring without rectal strictures, and therefore not of secondary nature. Dr. Joseph Goodman is reporting a short series of such cases from Johns Hopkins. Second, I believe that there is some evidence that there is a sarcoid form of this disease. I have seen two cases which were clinically and histologically characterististic of lymphopathia which had what appeared to be concomitant sarcoid lesions of the bones (i. e., cystic changes in the bones). In these cases there was no evidence of any other type of infection that could account for the sarcoid bone lesions.

DR. MAX S. WIEN, Chicago: To answer Dr. Tomlinson's question: The cutaneous phase may exist with gland involvement elsewhere in the body, but it is not essential that there be gland involvement contiguous to the areas of cutaneous ulceration. According to the concept of Chevalier and Bernard, histologically, in the pure cutaneous phase, one sees no evidence of involvement of the lymphatic network of the deep cutis; there is involvement high up in the cutis and involvement of the lymph spaces of the epidermis, whereas in the so-called adenopathic phase these deep glandular changes are not seen. In our first case the cutaneous ulceration occurred on the labia minora and labia majora, in areas apart from the inguinal gland involvement present. There was a lymphitis or lymphangitis of the involved sites. As to the specificity of the Frei test, commented upon by Dr. Robinson, there is no question in the minds of those who have done a large number of Frei tests about its specificity. We have done from 2,500 to 3,000 Frei tests and we feel that it is specific. One may get a positive Frei test with an asymptomatic lymphogranuloma inguinale just as one may get a seropositive asymptomatic syphilis. Positive Frei antigens have been produced in our case of lymphitis from maceration of the skin. Dr. Goldblatt brings up the point about Frei antigen giving a variable reaction. That is true of any antigen. It is an inherent property of antigens to give variable reactions. Hellerström brings out this fact and mentions that some antigens may be universal, giving the same type of reaction in all patients. Wherever there is lymphatic structure or lymphatic drainage, the virus of lymphogranuloma inguinale may go directly or by retrograde extension. We have seen erythema nodosum and erythema multiforme in the course of the disease. In testing a large series of cases

that were diagnosed chronic chancroidal infection with dmelcos antigen, we got one positive reaction proving that most of these cases were not chancroid. We feel that a large number of cases of chronic chancroidal infections which have not responded to the accepted treatment for chancroid will in the future be proved to be cases of the cutaneous phase of lymphogranuloma inguinale. As to the term lymphopathia venerea, we referred to Dr. Sulzberger's work in our previous papers and we are grateful to him for first calling our attention to this disease. We have adhered to the name lymphogranuloma inguinale to avoid confusion in the literature, because that is the name more frequently used. Ulcerative colitis and proctitis have occurred in our experience.

PARA-AMINO-BENZENE-SULFONAMIDE AND ITS DERIVATIVES

EXPERIMENTAL AND CLINICAL OBSERVATIONS ON THEIR USE IN THE TREATMENT OF BETA-HEMOLYTIC STREPTOCOCCIC INFECTION: A PRELIMINARY REPORT

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The recent observations of numerous European investigators [1] that para-amino-benzene-sulfonamide and certain of its chemical derivatives exert a specific chemotherapeutic effect in beta-hemolytic streptococcic infection are of great interest.

It will be our purpose in this preliminary communication to offer confirmatory observations to certain of the results already obtained by the aforementioned observers and to add new observations regarding the mode of action of these substances.

In the course of our investigations we have used two samples of para-amino-benzene-sulfonamide, one supplied to us by the Jackson Laboratory of E. I. DuPont de Nemours and Company, the other in tablet form under the name of "Prontylin" by the Winthrop Chemical Company. Two derivatives of para-amino-benzene-sulfonamide have also been studied. The first of these, the hydrochloride of 4′-sulfamido-2, 4 diamino-azo-benzene, was labeled "Prontosil tablets," while the second, the disodium salt of 4′-sulfamido-phenyl-2-azo-7-acetylamino-1 hydroxy naphthalene-3, 6-disulfonic acid, was sent to us in a liquid state, labeled "Prontosil —2.5 per cent Solution." Both of these preparations have been supplied to us by the Winthrop Chemical Company. The chemical structure of these products is presented in the structural formulas [2] on the opposite page.

We will not discuss the chemical properties of the substances except to state that in our experience the two preparations of para-amino-benzene-sulfonamide which we have used were soluble in water up to about 0.8 per cent and that, on standing, these substances tended to crystallize slowly out of solution. "Prontosil Solution," on the contrary, was a stable substance. "Prontosil Tablets" were relatively insoluble.

THE MODE OF ACTION OF PARA-AMINO-BENZENE-SULFONAMIDE AND ITS DERIVATIVES

In Vitro Experiments.—We have confirmed the observations of Colebrook and Kenny [2] that dilutions of "Prontosil Solution" had no effect on the growth of beta-hemolytic streptococci in 0.075 per cent dextrose beef-infusion broth or in 50 per cent normal horse serum broth. This is shown in tables 1 and 2. The bacterial growth in the tubes containing "Prontosil Solution" approximately equaled that in the control tubes.

However, when various concentrations of para-amino-benzene-sulfonamide were used a marked reduction in the growth of the streptococci was observed. This occurred not only in the broth cultures but also in the presence of 50 per cent normal horse serum broth. Attempts to test this bacteriostatic action in undiluted horse serum failed because we were unable to secure consistent growths of the organisms in that medium.

It is also interesting to note in this respect that a 1:10,000 concentration of para-amino-benzene-sulfonamide in serum broth markedly inhibited the growth of alpha hemolytic streptococci, gamma streptococci, pneumococcus types I and II, several varieties of Neisseriae from the throat, Micrococcus tetragenus, Haemophilus influenzae and Haemophilus haemolyticus. The growth of Staphylococcus aureus, typhoid bacilli, para A, para B, enteritidis, Flexner, Shiga and several other gram-negative bacilli was not affected by this concentration of the chemical.

It may be of some importance that the chemical seemed to exert a greater bacteriostatic action on one of the strains of hemolytic streptococci than on the other two. This difference between strain Ellis on the one hand and strains C203 and Schw on the other has been observed repeatedly.

From the Department of Medicine, the Johns Hopkins University Medical School.
Read in part before the thirtieth annual meeting of the Southern Medical Association, Baltimore, Nov. 17, 1936.
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The authors are indebted for cooperation to the visiting and house staffs of the various hospitals who have assisted in this investigation.

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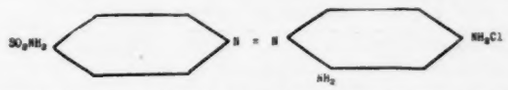
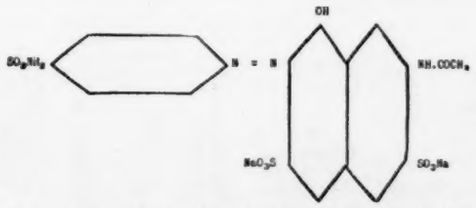
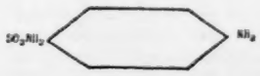
The mode of action of para-amino-benzene-sulfonamide in a 1 : 10,000 concentration in 50 per cent horse serum broth was of interest and is shown in the accompanying chart. Growth curves showed that in mediums inoculated with rapidly growing streptococci (twelve hour cultures) the bacterial population at the end of two hours' incubation was the same in the control medium and in the medium containing para-amino-benzene-sulfonamide. However, from this time a marked divergence in multiplication of the cocci occurred and the curve of the normal horse serum broth culture rose rapidly during the first twelve hours, while there was a distinct lag in the presence of para-amino-benzene-sulfonamide. At the end of twenty-four hours the peak of growth had been passed in the normal horse serum broth medium. In the medium containing para-amino-benzene-sulfonamide growth continued slowly through the second twenty-four hours and the curve continued to rise, without, however, touching that of the normal horse serum broth medium. Then growth stopped and the number of viable cocci markedly decreased but not, however, at the rate experienced by the cocci in the normal horse serum broth, thus making the curves meet and cross. This suggested the possibility that a slow multiplication of the cocci was still taking place in the medium containing para-amino-benzene-sulfonamide. Another explanation might be that, in the concentration used, the para-amino-benzene-sulfonamide was bactericidal to a certain degree.



Hydrochloride of 4 sulfamido-2, 4' diamino azo benzene (Prontosil).



Disodium salt of 4'-sulfamido-phenyl-2-azo-7-acetylamino-1-hydroxy-naphthalene-3, 6-disulfonic acid (Prontosil Solution).

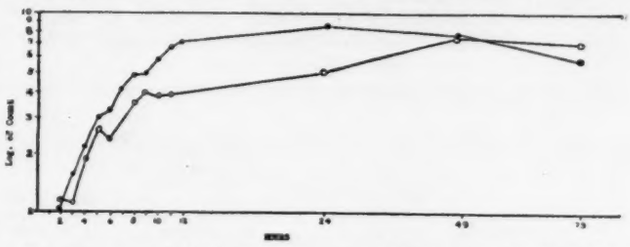


Para-amino-benzene-sulfonamide (Prontylin).

The chemical structure of para-amino-benzene-sulfonamide and its derivatives.

In Vitro and in Vivo Experiments.—Colebrook and Kenny [2] have pointed out that the serum of a patient ill with streptococcic puerperal sepsis becomes increasingly bacteriostatic after multiple doses of "Prontosil Solution." They also noted that the serum of a normal rabbit which had received a large intravenous injection of "Prontosil Solution" did not exhibit bacteriostatic qualities. We have frequently confirmed the second of these observations but have had difficulty in repeating the first. This has been due to the fact that the strains of hemolytic streptococci which we have employed in these tests are susceptible to the bactericidal effect of human serum. This phenomenon is of great importance in testing the growth of streptococci in human serum and has but recently been described by Tillett.[3]

The observation, however, that the normal rabbit cannot change "Prontosil Solution" to the active substance has seemed to us to be of great importance because it points toward the possibility that, for the



Growth curve of strain Ellis in normal horse serum broth and in normal horse serum broth containing para-amino-benzene-sulfonamide. Line with solid dots, 50 per cent normal horse serum broth; line with circles, 50 per cent normal horse serum broth + 1:10,000 para-amino-benzene-sulfonamide.

activation of "Prontosil Solution," infection with hemolytic streptococci, or changes brought about by infection, are necessary.

In order to test this hypothesis experimentally we first investigated the effects of high temperature on the activation of "Prontosil Solution" in vivo in the rabbit. Rabbit 271 in the incubator at 37 C. for several hours did not activate the "Prontosil Solution."

Then, following the suggestion of Dr. E. K. Marshall, we tested the effect of administering a strong reducing agent to rabbits previously injected with "Prontosil Solution." It was found that, if 2 Gm. of sodium formaldehyde-sulfoxalate in 20 cc. of distilled water was injected intravenously twenty minutes after 20 cc. of "Prontosil Solution" had been given by the same route, activation of the previously inert serum could be demonstrated. As will be seen in table 3, a definite degree of bacteriostasis was evidenced when streptococci were cultivated in the "Prontosil Solution"—sodium formaldehyde-sulfoxalate serum and that this power persisted to a minor degree over a period of twenty hours. In our experience the serum of rabbits injected with sodium formaldehyde-sulfoxalate alone did not show bacteriostatic serums.

These observations permit the postulation of the hypothesis that reduction is a factor in the activation of "Prontosil Solution." It is known [4] that hemolytic streptococci can, under certain conditions, bring about the reduction of some chemical substances. Certain preliminary observations which we have made suggest that this may explain the activation of "Prontosil Solution" in the presence of hemolytic streptococcic infection.

In Vivo Experiments.—There can be little doubt from the observations just recorded that activated "Prontosil Solution" and certain concentrations of para-amino-benzene-sulfonamide exert a distinct bacteriostatic effect in vitro and the assumption is that they act in a similar manner in vivo. However, it seemed to us that the results obtained in the treatment of infected mice (which will be described later) could not be attributed entirely to a bacteriostatic action on the part of these substances.

3. Tillett, W. S.: J. Exper. Med., to be published.
4. Hewitt, L. F.: London County Council Report No. 3116, ed. 3, p. 47.

We therefore studied the exudate obtained by peritoneal puncture from mice which had been infected nine hours prior to the first puncture and treatment. In table 4 the results of these observations can be seen. In the experiment here outlined, para-amino-benzene-sulfonamide was used as the therapeutic agent. Similar results have been obtained when "Prontosil Solution"

TABLE 1.—*Bacteriostatic Effect of "Prontosil Solution" and of Para-Amino-Benzene-Sulfonamide in Broth Cultures of Beta-Hemolytic Streptococci Incubated for Eighteen Hours*

Substance	Strain: Ellis Original Inoculum 0.1 Cc. of 1:500,000 Dilution of a 13 Hr. Broth Culture	Strain: C203 Original Inoculum Same as for Ellis
Broth	75,000,000	70,000,000
Broth + Prontosil S 1:100	20,000,000	50,000,000
Broth + Prontosil S 1:1,000	25,000,000	70,000,000
Broth + P.A.B.S. 1:10,000	4,000	3,000
Broth + P.A.B.S. 1:100,000	20,000	20,000
Broth + P.A.B.S. 1:1,000,000	3,000,000	2,000,000

P.A.B.S. = para-amino-benzene-sulfonamide.

TABLE 2.—*Bacteriostatic Effect of "Prontosil Solution" and of Para-Amino-Benzene-Sulfonamide in Broth Cultures of Beta-Hemolytic Streptococci Incubated for Eighteen Hours*

Substance	Strain: Ellis	Strain: C203	Strain: Schw.
Original inoculum	35	60	47
Normal horse serum (50% in broth)	240,000,000	250,000,000	260,000,000
N.H.S. + Prontosil S 1:100	180,000,000	380,000,000	100,000,000
N.H.S. + Prontosil S 1:1,000	170,000,000	250,000,000	
N.H.S. + P.A.B.S. 1:10,000	8,500	10,000,000	30,000
N.H.S. + P.A.B.S. 1:100,000	45,000	115,000,000	91,000,000
N.H.S. + P.A.B.S. 1:1,000,000	3,000,000	240,000,000	230,000,000

P.A.B.S. = para-amino-benzene-sulfonamide.

was employed. It is evident that phagocytosis of the streptococci by the polymorphonuclear leukocytes plays a paramount rôle in controlling the infection in the early stages of treatment and that later the monocytes join in this phenomenon. The following should be noted in respect to these experiments. Levaditi and Vaisman [5] believed that capsular production by streptococci was interfered with in the presence of these therapeutic agents. We were unable to confirm this observation.

We have noted already that, in vitro, the multiplication of streptococci was inhibited by para-amino-benzene-sulfonamide. It is possible that this may also occur in vivo, but in addition to this effect of the chemical we feel that the streptococci must also be damaged to permit such a marked degree of phagocytosis by the leukocytes. Thus, there is evidence that para-amino-benzene-sulfonamide and "Prontosil Solution" both inhibit the growth and injure hemolytic streptococci in the animal organism.

CURATIVE EFFECT OF "PRONTOSIL SOLUTION" AND PARA-AMINO-BENZENE-SULFONAMIDE IN EXPERIMENTAL BETA-HEMOLYTIC STREPTOCOCCIC INFECTIONS IN MICE

Our experience has been that a single prophylactic dose of 1 cc. of "Prontosil Solution" administered to mice, subcutaneously, twenty-four hours prior to infection by the intraperitoneal injection of from 100 to 1,000 minimum lethal doses of the strains C203, S24 or Schw was ineffective in protecting the mice against infection. While the survival time of the treated mice was longer than that of the untreated controls, no striking results were obtained. This result was to be expected because of the rapidity with which the "Prontosil Solution" was excreted in the urine.

In contradistinction to the prophylactic effects of "Prontosil Solution" the therapeutic effects of this substance were remarkable.

As noted in table 5, four different types of beta-hemolytic streptococci have been used in the therapeutic experiments. All the strains employed were at maximal mouse virulence; i. e., from 10^{-8} to 10^{-9} cc. of a twelve to fourteen hour blood broth culture regularly killed mice within forty-eight hours. It has been our experience with these strains during the past year that never has a mouse survived an intraperitoneal injection of 10^{-6} cc. of such a culture. This observation covered several hundred mice. Hence we feel reasonably certain that our results in this respect are completely valid. It is also of interest to note that with four exceptions all the 102 treated mice had positive blood cultures twelve hours after intraperitoneal inoculation.

In the preliminary experiments, the immediate survival rate in the treated mice was excellent. But, as can be seen, after the treatment was discontinued the mice began to die, some in the first few days, others as late as thirty days after the therapy had been discon-

TABLE 3.—*Effect of Parenteral "Prontosil Solution" on the Bacteriostatic Power of Rabbit Serum*

Serum	Results (Original Inoculum = 200 Organisms)
Rabbit 270 before treatment	715,000,000
Rabbit 270 after receiving Prontosil S intravenously (20 minutes)	700,000,000
Rabbit 271 before treatment but temperature 105.6 when bled	700,000,000
Rabbit 271 6 hours after receiving Prontosil S intravenously (temperature 106.0 when bled)	680,000,000
Rabbit 273 before treatment	800,000,000
Rabbit 273 after receiving Prontosil S intravenously (20 minutes)	1,000,000,000
Rabbit 273 after receiving Prontosil S and then (20 minutes) sodium formaldehyde sulfoxalate intravenously	65,000,000
Rabbit 273 after 20 hours	340,000,000

TABLE 4.—*Effect of Para-Amino-Benzene-Sulfonamide on the Peritoneal Exudate in Experimental Hemolytic Streptococcic Peritonitis in Mice* *

	Time of Examination of Peritoneal Exudate After Inoculation (Hours)	Therapy	No. of Colonies per Drop of Exudate	Differential Leukocyte Counts, Peritoneal Exudate: Polymorphonuclears	Lymphocytes	Monocytes	% Polymorphonuclears Showing Phagocytosis	% Monocytes Showing Phagocytosis
Mouse 1	9	9 mg.	Innumerable	70	9	21	0	0
	12	9 mg.	Innumerable	58	0	42	0	0
	26	9 mg.	Innumerable	77	4	19	54	20
	50	9 mg.	200	65	3	32	32	30
	74	9 mg.	80	28	9	63	25	55
	98	9 mg.	5	30	0	70	3	6
	122	9 mg.	0	15	19	63	0	1
	146	9 mg.	0	12	24	64	0	0
	170	9 mg.	0	17	20	63	0	0
	218	.....	0	14	30	56	0	0
Mouse 2	9	None	Innumerable	48	29	23	0	2
	12	None	Innumerable	40	45	15	0	0
	26	None	Innumerable	40	32	28	0	0
Dead 28 hrs.								

* Inoculum 100-1,000 MLD C_{203} intraperitoneally.

5. Levaditi, C., and Vaisman, A.: Compt. rend. Acad. d. sc. **200:** 1694 (May 13) 1935; Compt. rend. Soc. de biol. **119:** 946, 1935.

tinued. In this respect our results differed from those reported by Colebrook and Kenny and others.[6]

Because of an interval of generally twelve hours between the second and third treatments, we decided to infect two large groups of mice, one with strain C203, the other with strain Schw, and to treat them at four hour intervals for a period of sixty hours after the commencement of the therapy. By doing so we hoped to approach the treatment schedule which is followed in severe human cases. Then after this intensive period of early treatment we planned to taper off the therapy gradually over a two weeks period.

This plan seemed to work very well in practice, because in the C203 group of treated mice there were but six deaths and in the Schw group seven deaths from streptococcic infection during the first two weeks. However, after the cessation of treatment, deaths from streptococcic infection appeared in both groups, although to a lesser degree than in the first groups of treated mice.

When solutions of para-amino-benzene-sulfonamide were used in the treatment of these experimental infections in mice, the results seemed to be a little better than those obtained with "Prontosil Solution." The immediate survival rate was definitely augmented and more mice have survived over a period of thirty days. These observations are in harmony with those described by several European investigators.[7]

The explanation of these late deaths after therapy has been discontinued can be made clear. One must remember that the white mouse lacks any natural resistance to intraperitoneal infection with multiple lethal doses of a strain of hemolytic streptococcus of maximal virulence. It always dies. Neither is it easy to immunize these mice against these same virulent strains. We have tried repeatedly to immunize mice with C203 and Schw vaccines without obtaining a degree of immunity capable of offering resistance to 100 lethal doses of the homologous strains. With these facts in mind, one can understand why the mice die after treatment has ceased. Unless the infecting agent has been completely eradicated, the mouse will probably succumb.

TABLE 5.—*Curative Effects of "Prontosil Solution" and of Para-Amino-Benzene-Sulfonamide in Experimental Beta-Hemolytic Streptococcic Injections in Mice*

Strain of Beta Hemolytic Streptococci	No. of Mice	Amount of Inoculum	Treatment Commenced, Hrs. After Infection	Time of Tail Blood Culture, Hrs. After Infection	Blood Culture: No. Positive	Blood Culture: Average Colonies per Cc.	Therapeutic Agent	Days of Treatment	Total Dosage (Mg. of Chemical)	Deaths in Each 24 Hour Period: 1	2	3	4	5	6	7	Deaths in Periods of Days: 8-11	12-16	17-23	24-30	31-38	39-48	49-64
Da	6	0.000001, 100 to 1,000 MLD	8	12	6	130	P.S.*	5	125	..	..	..	..	..	..	..	+++	+	..	..	+	..	..
Da	8	0.000001, 100 to 1,000 MLD	Untreated control mice							+++	+++ ++	..	..	..	..	..	..	..	..	..	..	..	..
C203	6	0.000001, 100 to 1,000 MLD	8	12	6	1,225	P.S.	6	181	..	++	..	..	..	..	..	..	+++	..	..	0	..	..
C203	6	0.000001, 100 to 1,000 MLD	8	12	6	1,693	P.S.	7	156	..	+0	..	..	+	..	..	..	+0	..	..	..	..	..
C203	24	0.000001, 100 to 1,000 MLD	8	12	24	1,300	P.S.	14	285	..	++ +	0	..	++	..	..	+	+++	+	..	0	..	..
C203	20	0.000001, 100 to 1,000 MLD	Untreated control mice							+++++ +++++ +++++	++ + ++	..	..	..	..	..	..	..	..	..	..	..	..
S24	6	0.000001, 100 to 1,000 MLD	8	12	6	395	P.S.	6	150	..	..	..	..	+	..	..	+++	+	..	..	0	..	..
S24	6	0.000001, 100 to 1,000 MLD	Untreated control mice							++ +++	+	..	..	..	..	..	..	..	..	..	..	..	..
Schw.	6	0.000001, 100 to 1,000 MLD	8	12	6	880	P.S.	7	155	..	++	..	..	..	..	..	+	..	..	+	+	+	..
Schw.	6	0.000001, 100 to 1,000 MLD	8	12	6	5,440	P.S.	7	160	..	++	..	..	..	..	..	+++	..	..	..	..	..	..
Schw.	24	0.000001, 100 to 1,000 MLD	8	12	22	978	P.S.	14	285	..	++ +	.. ++	..	..	..	..	.. ++	.. 0+	+++ +0+	0000 +	..	..	..
Schw.	20	0.000001, 100 to 1,000 MLD	Untreated control mice							+++ ++ ++	+++ +++ +++ +++ +	..	..	..	..	..	..	..	..	..	..	..	..
C203	6	0.000001, 100 to 1,000 MLD	8	12	4	802	P.A.B.S.†	7	90	..	..	..	..	..	..	..	++	++	..	..	..	..	..
C203	6	0.000001, 100 to 1,000 MLD	8	12	5	383	P.A.B.S.†	7	117	..	..	..	+	..	..	..	+	..	..	..	..	..	..
C203	6	0.000001, 100 to 1,000 MLD	8	12	6	908	P.A.B.S.‡	7	117	..	..	..	..	..	..	..	..	..	..	..	..	..	..
C203	10	0.000001, 100 to 1,000 MLD	Untreated control mice							+++ +++ ++	++	..	..	..	..	..	..	..	..	..	..	..	..

* "Prontosil Solution."
† Para-amino-benzene sulfonamide (DuPont).
‡ Para-amino-benzene-sulfonamide ("Prontylin") (Winthrop).
+ Died of beta-hemolytic streptococcic infection.
0 Died of another infection (mostly mouse typhoid).

6. Domagk, Gerhard: Angew. Chemie **48**: 657,1935; **61**: 250 (Feb. 15) 1935. Levaditi and Vaisman.[5] Colebrook and Kenny.[2] Buttle, Gray and Stephenson.[7]

7. Buttle, G. A. H.; Gray, W. H., and Stephenson, D.: Protection of Mice Against Streptococcal and Other Infections by *p*-aminobenzenesulfonamide and Related Substances, Lancet **1**: 1286 (June 6) 1936. Colebrook and Kenny.[2]

We have obtained results similar to those reported by Colebrook and Kenny and others [7] when we attempted to treat experimental mouse infections produced by hemolytic streptococci of low mouse virulence. We could prolong the survival period of the treated mice over that of the untreated mice but were unable to influence the final mortality rate in the treated animals. we have attempted to evaluate its curative effects in patients ill with beta-hemolytic streptococcic infections.

It is always necessary in testing new therapeutic agents to adopt a skeptical attitude toward the results obtained. Too often have early brilliant therapeutic successes eventually proved to be due to chance or to optimism of the reporter. Bearing this in mind, it is possible that the good clinical results observed by us after administration of para-aminobenzene-sulfonamide and its derivatives were due to chance; but it is not possible that the results in treatment of experimental infections were. Therefore we believe that continued clinical observations of the effect of these substances in the treatment of hemolytic streptococcic infections in human beings should be vigorously prosecuted.

TABLE 6.—*Summary of Nineteen Cases Treated with Para-Amino-Benzene-Sulfonamide and Its Derivatives.**

Patient	Diagnosis	Sex Age	Duration of Disease (Days)	Bacteriologic Culture	Prontosil, Gm. Parenteral	Prontosil, Gm. Orally	Prontosil, Gm. Total	Day of Administration	Other Observations
1	Infected abortion; pelvic peritonitis	♀ 33	9	Uterus-beta-hemolytic streptococcus	1.75	13.2 Prontosil	14.95	9	Gravely ill; hb., 6.4 Gm.; W.B.C., 4,850; temp., 106.4 F. on day of treatment; two transfusions of citrated blood; temperature normal 17 hrs. after beginning of treatment; recovery from infection uneventful.
2	Erysipelas of left leg	♂ 2	1	B.H.S.; staphylococcus aureus	1.4	18.9 Prontylin	20.3	13	Temperature normal 48 hrs.; lesion did not advance after first treatment; oral administration for furunculosis; erysipelas lesions disappeared rapidly
3	Scarlet fever	♂ 14	1	B.H.S.	2.2	22.2 Prontosil	24.2	11	Temperature normal in 36 hrs.; throat cleared with great rapidity; uneventful convalescence
4	Erysipelas; lymphangitis, left leg	♀ 36	1	B.H.S. in lesion and blood stream	3.75	28.8 Prontylin	32.55	10	Temperature normal in 60 hrs.; erysipelas lesion disappeared rapidly; leg ulcer healed rapidly
5	Acute tonsillitis	♀ 24	3	B.H.S.	2.5	15.0 Prontylin	17.5	4	Temperature normal in 30 hrs.; throat normal in 48 hrs.; discharged on 5th day with throat culture negative for B.H.S.
6	Chronic cystitis and cervicitis	♀ 36	?	B.H.S., group B	....	10.8 Prontosil	10.8	3	Urine became free from streptococci; recurrence 1 week after treatment; insufficient treatment
7	Infected traumatic injury, left eyeball; enucleation, left eye	♂ 44	2	B.H.S.; staphylococcus aureus; B. coli	3.25	18.0 Prontylin	21.25	7	Temperature normal in 48 hrs.; recovery uneventful
8	Traumatic injury left eye; purulent panophthalmitis; enucleation of left eye	♀ 3	2	B.H.S.	2.1	.....	2.1	2	Temperature normal in 48 hrs.; recovery uneventful
9	Chronic impetigo	♀ 2	3½ mos.	B.H.S.; staphylococcus aureus	....	42.0 Prontylin	42.0	15	Had resisted all therapy; lesions began to clear after Prontylin administration; lesions negative for B.H.S. within 4 days after institution of Prontylin therapy
10	Erysipelas, left leg	♀ 7	9	.....	1.25	4.2	5.45	3	Child gravely ill; erysipelas lesion spreading despite transfusions and antitoxin; temperature normal in 28 hrs.; recovery uneventful
11	Erysipelas, right leg; bronchopneumonia	♀ 3	1	B.H.S.	....	.....	.....	..	Temperature normal in 48 hrs.; lesion disappeared rapidly, as did also the bronchopneumonia
12	Erysipelas, right ear; otitis media right ear; essential hypertension	♂ 35	5	.....	2.25	.....	2.25	2	Patient was recovering when drug was administered
13	Bilateral otitis media; erysipelas, right ear; bilateral maxillary sinusitis	♂ 58	4	B.H.S.	1.5	57.0 Prontylin	58.5	10	Temperature normal in 40 hrs.; erysipelas lesion disappeared rapidly; marked decrease in discharge from ears; right antrum drained on fifth day; uneventful recovery
14	Ludwig's angina	♂ 70	8	.....	3.25	.....	3.25	1	Died 22 hours after first parenteral injection
15	Cellulitis of legs; septicemia	♂ 57	7	Blood culture (40 colonies of B.H.S. per cc. of blood	2.5	.....	2.5	1	Died 9 hours after first parenteral injection
16	Acute bilateral otitis media and mastoiditis; septicemia	♂ 5	?4	Blood culture 2,150 colonies of B.H.S. per cc. of blood	11.75	.....	11.75	13	Gravely ill; possible right jugular thrombosis; meningismus; developed metastatic infections in both elbows and over right clavicle; blood culture negative on 5th day; hemoglobin fell to 40%; 3 transfusions after negative blood culture; sterile pleural effusion eleventh day; temperature normal 18th day discharged 26th day
17	Scarlet fever; cervical adenitis	♀ 6	9	Blood and cerebrospinal fluid negative	5.25	.....	5.25	4	Marked meningismus with 400 cells in C.S.F.; glands decreased rapidly; temperature fell to normal in 6 days
18	Scarlet fever; cervical adenitis; bilateral otitis media	♀ 6	18	.....	....	5.4 Prontosil	5.4	3	Septic type of temperature up to 104; multiple myringotomies both ears with abundant purulent discharge; temperature fell to normal in 24 hours; ears clear in 3 days
19	Acute follicular tonsillitis; right peritonsillar abscess	♂ 22	6	B.H.S.	2.5	7.2 Prontosil	9.7	4	Marked decrease in swelling and edema within 40 hrs.; temperature normal in 40 hrs.; abscess ruptured (?) at 36 hrs.; patient discharged 5 days after admission

* Seven other patients have been treated with para-amino-benzene-sulfonamide and its derivatives since this table was prepared.

THE CLINICAL USE OF "PRONTOSIL SOLUTION," "PRONTOSIL TABLETS" AND PARA-AMINO-BENZENE-SULFONAMIDE

In view of the very definite therapeutic effect of para-amino-benzene-sulfonamide and its derivatives on experimental hemolytic streptococcic infection in mice and because of the encouraging reports of their use by European clinicians in human streptococcic infections,

TOXIC EFFECTS

In the course of observations on the patients presented in this report we have noted that the therapeutic agents employed are relatively nontoxic. The intravenous injection of "Prontosil Solution" frequently resulted in nausea, vomiting and an immediate bowel movement. As we have found that following a subcutaneous injection of "Prontosil Solution" the substance appears in the urine in fifteen minutes, we are of the opinion that the intravenous use of the product is unnecessary. We have not observed any changes in the urine, white blood cell count or red blood cell count that could be attributed to the therapeutic agent. None of our patients developed sulfemoglobinemia. We have been insistent that no saline laxative be used while a patient is under treatment. The only known toxic manifestation was that of fever. When a large dose (100 cc.) of "Prontosil Solution" was administered under the skin in a normal human being the temperature mounted to from 102 to 103 F. (rectal) in from eight to twelve hours. This fever lasted twelve hours and then the temperature declined rapidly to normal. A feeling of lassitude and slight frontal headache was experienced by the subject during the febrile period. This reaction was not observed in patients who received smaller divided doses of "Prontosil Solution" but has been observed in those who received a single large dose. No toxic symptoms were observed in mice that had received large amounts of "Prontosil Solution" over a long period of time.

The samples of para-amino-benzene-sulfonamide that we tested were definitely toxic for mice. A subcutaneous injection of 9 mg., repeated after a three hour interval, produced in the animals symptoms of a bilateral vestibular dysfunction and a curious spastic paralysis. However, within four hours these symptoms disappeared and the mice appeared as healthy as ever. In patients, long continued therapy with this substance did not result in toxic manifestations.

DOSAGE

When "Prontosil Solution" is used, we feel that it is important to administer a large amount during the first twenty-four hours of treatment. Hence we have adopted the following measure for determining total dosage during the first twenty-four hours of treatment: For each pound of body weight up to 100 pounds (45 Kg.) we advise 1 cc. of the substance. Between 100 and 150 pounds (68 Kg.) the total first day dose is 100 cc. For patients weighing over 150 pounds the dose is determined on the basis of 0.75 cc. per pound (450 Gm.) of body weight. After the first twenty-four hours the total daily dose should be about one half of the amount administered in the first twenty-four hours except in patients suffering from beta-hemolytic streptococcic septicemia. In these individuals the original amount should be continued until the blood stream is sterile.

As it has been shown that para-amino-benzene-sulfonamide in a concentration of 1 : 10,000 is bacteriostatic in vitro, we have tried to attain a high concentration in the patients treated with this substance. We know little about the absorption and nothing about the excretion of this drug. However, we have found that some patients will tolerate a gram of para-amino-benzene-sulfonamide for each 20 pounds (9 Kg.) of body weight per day for at least one month.

When para-amino-benzene-sulfonamide is used orally in conjunction with "Prontosil Solution" parenterally, one should decrease the estimated parenteral dose by 20 cc. for every gram of para-amino-benzene-sulfonamide administered. When one is administering either "Prontosil Solution" or para-amino-benzene-sulfonamide to patients, the total calculated daily dose should be divided into four parts and given at intervals of six hours.

Finally, it should be remembered that saline laxatives and cathartics should not be administered during the period in which these substances are being used as therapeutic agents.

SUMMARY AND CONCLUSIONS

In view of the experimental evidence presented, we believe that the careful clinical use of para-amino-benzene-sulfonamide and its derivatives in the treatment of human beings ill with infections due to beta-hemolytic streptococci is warranted.

CARCINOMA OF THE RECTUM

FACTORS AFFECTING ITS CURE

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Several facts pertain to cancer of the rectum which favorably influence the prognosis. A more optimistic view with regard to malignant conditions here should prevail. Practically all patients with carcinoma of the rectum can be cured when adequate surgery is instituted in the early stages of the disease. Rectal cancers can be diagnosed easily and with certainty while the lesion is early and curable. This ideal falls far short of attainment. Lahey [1] believes that one patient in four with this condition can be relieved by surgery. Miles [2] reports 21 per cent of five-year cures for all cases seen presenting a rectal malignant growth. Fansler [3] writes that not more than 40 or 50 per cent of those patients are suitable for radical operation. Dixon,[4] reviewing a large series at the Mayo Clinic, states that in more than 50 per cent of the cases the growths were inoperable. Bowing and Fricke,[5] analyzing the end results of the treatment of 500 patients by the combined measures of surgery and radiation therapy, report 22.53 per cent of five year good results. Many facts concerning this disease make it possible for a larger percentage of patients with a rectal malignant condition to obtain relief. A discussion, therefore, of some of the factors that modify the probability of cure of the patient with carcinoma of the rectum seems timely. The records at the Scott and White Clinic of 167 patients having cancers of the rectum have been reviewed, and the study forms the basis for the conclusions in this presentation.

The extent of the neoplasm is the most important modifying factor. Cancer of the rectum, early, as

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3. Fansler, W. A.: Carcinoma of the Rectum, Journal-Lancet **52:** 255 (April 15) 1932.
4. Dixon, C. F.: Treatment and Prognosis of Cancer of the Rectum, Illinois M. J. **68:** 89-93 (July) 1935.
5. Bowing, H. H., and Fricke, R. E.: Primary Rectal Carcinoma Under Radium Treatment, Am. J. Roentgenol. **32:** 635 (Nov.) 1934; Preoperative Radium Treatment of Rectal Carcinoma, Sec. Therap. Radiology, Mayo Clinic. Bowing, H. H.; Fricke, R. E., and Harper, F. R.: Treatment of the Carcinoma of the Rectum by Radium, Am. J. Roentgenol. **25:** 644 (May) 1931.

cancer elsewhere in the body, is a local lesion and while in this stage of development is readily amenable to surgical removal, with the probability of permanent relief. The carcinoma begins in the mucous membrane from the crypts or glands of Lieberkühn as a node of proliferating, abnormal epithelium. It arises frequently from an adenoma or a papilloma, and according to Rosser [6] sometimes from an ulcer, a fissure or a fistula or from leukoplakia.

How long does a rectal cancer remain a local lesion? Its first method of spread is by continuity of tissue as the growth develops. The next is by metastasis through the lymphatics, and occasionally the cancer cells are disseminated by the blood stream. Lymphatic invasion and distant venous metastasis seldom take place before the muscular coats of the intestine have become deeply invaded or until after the lesion has grown entirely through its wall. Certainly the more deeply the lesion has penetrated into the intestinal wall, the greater the probability of metastasis. Gordon-Watson [7] writes: "It is probable that the state of lymphatic invasion is seldom reached under six months and usually takes longer." Miles states, "Direct extension through the muscular coat of the bowel appears to be a slow process and the fascia propria of the rectum is not usually invaded until the disease has existed for eighteen months." Wilkie [8] believes that cancer of the rectum remains a local disease probably at least a year.

It is impossible to ascertain the exact time at which a cancer of the intestine begins. Probably most of the growths have existed a few months before suggestive signs and symptoms were in evidence. Most lesions, therefore, are of a definitely longer duration than the patient's history would seem to indicate. In this study I found the average duration of symptoms for the patient with an operable malignant growth to be 9.4 months. One patient of the operable group gave a history dating back twenty-four months. The average duration of symptoms of those cases considered inoperable when first examined was fourteen months. Rankin [9] finds in the average case of rectal carcinoma that symptoms have been present about eleven months. Since the extent of the lesion is an important factor affecting the cure, it is an encouraging fact to know that for a majority of patients the cancers are local, removable and curable for many months.

The time at which the diagnosis is made is a vital factor, for it determines the extent of the carcinoma. This is also the one factor about which most can be done toward increasing the number of cures. Therefore an endeavor should be made to diagnose more early lesions. The symptoms and signs of early disease should be remembered. Blood in the stool is the most important first indication of cancer, and a mild rectal discomfort is next. The patient describes this as an uneasiness, a heaviness, a weighty feeling, a soreness or a mild cramping. Intense pain is practically never an early manifestation of this disease. A history of bleeding was given by 80 per cent of these patients, and the complaint of a rectal discomfort was made by 68 per cent. A change in bowel habit may be the earliest symptom. These few signs and symptoms are sufficient to cause rectal cancer to be suspected, and, when suspected, a careful digital and proctoscopic examination should be made. Practically all rectal cancers can be diagnosed by these two simple procedures. Wheeler [10] states that 90 per cent of rectosigmoidal and rectal cancers can be diagnosed by digital palpation. Bargen [11] writes that about 95 per cent of all rectal lesions are within reach of the examining finger and concludes that delay by the physician in making a digital examination is one of the chief factors contributing to the poor prognosis of carcinoma of the rectum. Certainly if digital and proctoscopic examinations with biopsy were done always on patients with such complaints, more early diagnoses would be made and the resulting number of cures for patients with rectal carcinoma would be materially increased. Lockhart-Mummery [12] states that more than 75 per cent of cures can be expected when the diagnosis is made early. Abel's [13] statistics show that 77 per cent of patients are free from recurrence five years after surgical extirpation when the operation is performed early before the glands become involved.

The size of the lesion is to be taken into consideration, since it is somewhat of an index to the duration of the disease. Cutting [14] stated that a carcinoma which has encircled three fourths of the intestine is of about one year's duration, while Miles believes that it probably requires eighteen months for a tumor to reach such an extent. The size of the neoplasm, however, is a poor index of its curability. Frequently the prognosis is more hopeful for the case presenting a large tumor than for the one presenting a smaller neoplasm. Pfeiffer [15] states that the size of the growth bears no necessary relation to metastasis; in fact, the relation is more likely to be inverse. McVay [16] also finds the tumors without glandular involvement to be about average in size. Several patients of our series with tumors 7 or 8 cm. in diameter have remained well after surgical extirpation, while, in contrast, others with cancers only 3 or 4 cm. in size have developed a recurrence following their operation. The explanation for the end results in these cases is to be found in the degree of activity of the malignant cell and in the different clinical varieties of rectal cancer. Three different kinds are seen: the papilliferous, the adenoid and the colloid. The papilliferous grows rapidly on the surface and may involve the entire circumference of the intestine and protrude into and fill its lumen, producing a very large tumor before there is deep invasion of the muscular coats by malignant cells. Therefore the papilliferous, fungating, protuberant neoplasm, growing chiefly into the intestinal lumen, metastasizes slowly and, even though a very large tumor has developed, is still a favorable lesion for removal; on the other hand, the ulcerating cancer of the adenoid or colloid variety which has penetrated deeply into the rectal wall, even though small, is frequently highly

6. Rosser, Curtice: The Etiology of Anal Cancer, Am. J. Surg. **11:** 328-333 (Feb.) 1931

7. Gordon-Watson, C.: Treatment of Cancer of Rectum with Radium by Open Operation, Proc. Roy. Soc. Med. **21:** 9 (Dec.) 1927. Gordon-Watson, C., and Regand, C.: Discussion on Radium Treatment of Malignant Disease of Rectum and Anus, ibid. **28:** 1251-1263 (July) 1935.

8. Wilkie, D. P. D.: Excision of Rectum for Carcinoma, Surg., Gynec. & Obst. **48:** 677 (May) 1929.

9. Rankin, F. W.: The Diagnosis and Treatment of Carcinoma of the Rectum and Rectosigmoid, South. Surgeon **1:** 247 (Oct.) 1932.

10. Wheeler, W. I. de C.: Early Diagnosis of Carcinoma of Colon and Rectum, Irish J. M. Sc., pp. 579, Sept. 1928.

11. Bargen, J. A., and Leddy, E. T.: Carcinoma of Rectum: Causes for Poor Prognosis, J. A. M. A. **104:** 1201-1203 (April 6) 1935.

12. Lockhart-Mummery, J. P.: Excision of Rectum for Cancer, Am. J. Cancer **18:** 1-14 (May) 1933.

13. Abel, A. L.: Cancer of Rectum: Five Year Cures by Radical Abdominoperineal Excision, Surg., Gynec. & Obst. **60:** 481-482 (Feb., No. 2A) 1935.

14. Cutting, R. A.: Carcinoma of Anus and Rectum, Am. J. Surg. **10:** 547-556 (Dec.) 1930.

15. Pfeiffer, D. B.: The Principles Underlying the Surgery of Carcinoma of the Rectum, Ann. Surg. **86:** 374-387 (Sept.) 1927.

16. McVay, J. R.: Involvement of Lymph Nodes in Carcinoma of Rectum, Ann. Surg. **76:** 755 (Dec.) 1922.

malignant, may metastasize early, and often tends to recur after wide removal. The size of the tumor, therefore, is a poor index to its curability.

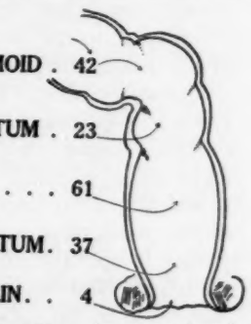
The pathology of rectal neoplasms is quite an important factor influencing the probability of cure. A specimen for biopsy can be obtained readily when the proctoscopic examination is being done. By this procedure the diagnosis usually can be definitely confirmed and the degree of malignancy ascertained. Occasionally the biopsy does not show the correct grade of cell activity and may fail even to demonstrate the presence of cancer. This probably is due to the fact that the section failed to include any of the actual tumor, or to changes in the tissue produced by degeneration and infection. A negative report, therefore, does not exclude carcinoma. Specimens have been obtained for pathologic study from 124 patients. Twenty-six of these were of the papillary variety, four were of the colloid variety, ninety-one were adenocarcinoma (simplex) and three were squamous cell epitheliomas.

A study of the degree of malignancy, based on cell differentiation as advocated by Broders, was made, and it was found that nine carcinomas were grade 1, fifty-five were grade 2, forty-eight were grade 3 and five were grade 4. The character of specimens obtained from seven lesions did not permit of grading. Sixty-four of the 117 cancers graded, or 54.7 per cent, were found to be either grade 1 or grade 2 in degree of malignancy. Bowing and Fricke report 70 per cent are in the grade 1 and grade 2 groups. Hayden and Shedden,[17] with a somewhat different method of grading, state that 77 per cent of rectal cancers are in the lower grades of malignancy. These neoplasms of grades 1 and 2 are slow to metastasize and, by wide surgical removal of such lesions, a high probability of cure may be expected. It is a fortunate fact, favorably influencing prognosis, that a definite majority of rectal carcinomas have a low degree of activity of the malignant cell.

Seventy of the seventy-six specimens obtained by removal of the growth permitted examination with reference to the depth of penetration of the intestinal wall by cancer and also with regard to the frequency of demonstrable glandular metastasis. The lesion was found superficial to the muscle in twenty-one specimens. The muscles were invaded by carcinoma cells in ten, and in forty-seven the cancer had penetrated through the intestinal wall to or beyond the serosa. That is, the carcinoma had invaded into or through the muscular coats in fifty-two of the seventy-three cases, or 71.2 per cent. The depth of penetration of the carcinoma into or through the intestinal wall definitely affects the probability of glandular metastasis and therefore the likelihood of cure. Dukes[18] states that as a rule lymphatic dissemination does not play any part in the spread of cancer of the rectum until the growth has penetrated by direct continuity into the perirectal tissues.

Glandular metastasis was demonstrated in only sixteen of the seventy specimens, or 23 per cent. Jones and McKittrick[19] found glandular metastasis in only 32 per cent. MacCarty[20] made a study of 1,826 rectal and sigmoidal carcinomas and reported glandular involvement in 38 per cent. Dukes made a study of 100 cases and reported glandular involvement in forty. McVay, in a very detailed examination of 100 resected rectums, demonstrated metastasis to the glands in forty-seven. Such statistics indicate that rectal carcinoma is slow to metastasize to lymph glands and that for a majority of the patients the cancer remains local until late. Glandular metastasis markedly affects the curability. Rankin and Broders[21] report only 20.68 per cent of good results when the glands were involved and 57.87 per cent of good results when the glands were free.

The degree of malignancy should be considered in selecting the type of operation to be performed. Sometimes the grade of the cancer will be the determining factor in deciding operability. Certainly all definitely extirpable carcinomas of the rectum should be treated surgically. Surgery, however, should be advised more often for the more advanced or borderline lesions of the lower grades than would be considered for the higher degrees of malignancy of the same extent. Neoplasms of a highly malignant degree and of the borderline operability are treated preferably by radium and roentgen rays rather than by surgery. Radiation therapy is indicated for many of the extensive anal epitheliomas. However, a posterior hot-knife excision of the rectum is the preferable treatment for all operable squamous cell lesions of this location. A knowledge of pathology, therefore, is an invaluable aid in determining the preferable method of treatment. There are also four factors related to pathology which materially affect the prognosis. They are the different clinical varieties of cancer, the degree of activity in the carcinoma cell, the depth of penetration of the intestinal wall by malignant tissues and the presence or absence of glandular involvement.



Location of the 167 carcinomas reviewed in this study.

The mobility of the growth is a very important factor influencing the treatment. All movable lesions are extirpable, and proper surgical excision offers to such patients the most for a favorable prognosis. Restriction in the mobility of the neoplasm decreases the operability, increases the hazard of surgical treatment and diminishes the probability of permanent relief. However, when a lesion is fixed it is important to remember that the fixation may be due to accompanying inflammatory changes rather than to an extension of the disease. The enlargement of the regional lymph glands is due frequently to a simple adenitis rather than to a metastatic malignant growth. Sometimes after a colostomy, by putting at rest the diseased intestine and by local treatments, the inflammatory changes subside and a cancer that apparently was fixed and inoperable becomes mobile and removable. Gordon-Watson also reports that some immobile neoplasms will be converted into operable tumors by radiation therapy.

The sex of the patient has a bearing on the cure to a slight degree. The prevalence of rectal cancer is

17. Hayden, E. P., and Shedden, W. M.: Carcinoma of the Rectum, Surg., Gynec. & Obst. **51**: 783 (Dec.) 1930.
18. Gordon-Watson, C., and Dukes, C.: The Treatment of Carcinoma of the Rectum, Brit. J. Surg. **17**: 643 (April) 1930; abstr., Internat. Abstr. Surg., Surg., Gynec. & Obst. **51**: 309 (Oct.) 1930.
19. Jones, D. F., and McKittrick, L. S., Tr. Am. S. A., 1922, pp. 139-359.
20. MacCarty, W. C.: Size of Operable Cancers, Division of Surgical Pathology, Mayo Clinic.
21. Rankin, F. W., and Broders, A. C.: Factors Influencing Prognosis in Carcinoma of the Rectum, Surg., Gynec. & Obst. **46**: 660-667 (May) 1928.

higher in the male. Buie [22] finds that 64 per cent are of the male sex. Pfeiffer states that the ratio is almost that of two to one. There were ninety-five males and seventy-two females in this group which was reviewed. That is, 57 per cent were males and 43 per cent were females. The pathology is not influenced, apparently, by the sex. Owing to the narrower male pelvis, surgical removal of a rectal neoplasm for him is more difficult and the pelvic peritoneum of the man is less resistant to infection than is that of the woman. Because of these facts, surgical extirpation of the rectum carries a higher mortality for the male. Sir George Newman [23] reports that the prospects of survival are better for women than for men after radical operation. Yeomans [24] states that the mortality is 7 per cent greater for men.

The age of the patient definitely affects the prognosis. The youngest patient in this group was 23; the oldest was 84. There were five patients in the third decade of life, sixteen in the fourth, thirty-three in the fifth, forty-five in the sixth, thirty-nine in the seventh, twenty-six in the eighth and three in the ninth. The tissues of the young are more elastic and have a richer blood supply, and their lymphatics are more open, factors that are favorable to the rapid growth and dissemination of a neoplasm, while the fibrotic, sclerosing changes accompanying senescence tend to retard the development and spread of a malignant condition. Therefore, in the young the lesion is usually of a high grade malignancy and of a more rapid growth and metastasizes early. Pathologic specimens were obtained from sixteen patients under 40 years of age. A study of these showed two to be grade 1, four to be grade 2, eight to be grade 3 and two to be grade 4. That is, practically two thirds of the patients under 40 had highly malignant tumors. When the neoplasm in the young is operable, it should be removed together with all lymph bearing tissue after the most thorough manner. Three patients under 40 were operated on now more than five years ago. Two of these are alive now, one eight years and one five years after the malignant growth was removed. Lockhart-Mummery writes: "I have no record of any patients under 30 who has not died from prompt recurrence." Mechling [25] states that a patient under 30 years of age does not recover from rectal cancer. Unquestionably the prognosis is grave for the young patient with carcinoma of the rectum.

The physical condition of the patient modifies the treatment and prognosis. All surgery is precluded for some on account of their age, and for others because of disease of either the heart, kidneys or lungs or some other debilitating illness; and only a restricted operation should be advised for some others, because of the hazard of a more radical surgical procedure. It is seldom necessary, however, that the benefits offered by surgical treatment be denied a patient with cancer of the rectum because of his physical status. A great deal can be done to rehabilitate the poor risk. Rest, foods, fluids, dextrose, blood transfusions and encouragement will do much to prepare such patients for an operation. There were four patients over 70 years of age for whom a radical removal of the rectum was performed and two others for whom a wide local excision of the lesion was done, and all had a satisfactory convalescence.

The mental attitude of the patient can be an important factor. Some are not willing to accept a colostomy, even though it would permit a safer and wider removal of their disease. For such patients the surgeon should be willing to give due consideration to other therapeutic measures or to other surgical procedures that will permit either the restoration of intestinal continuity or the making of a posterior anus. Some patients assume that their condition is hopeless and are unwilling to make the effort to get well. This is true of a few even after they have accepted surgery. There were twenty-two of this series who declined the aid offered by surgery. Radiation therapy offers the most to the patients who assume such an attitude.

The location of the lesion must be given consideration, for the pathologic types vary in the different parts of the intestine and the symptoms are modified by the portion that is involved. The smallest caliber of the large intestine is in the rectosigmoid. The cancer often grows along the blood and lymph vessels around the inside of the intestinal wall, producing annular, constricting tumors. The small caliber of the bowel and the nature and development of the neoplasms here fortunately tend to a rather early manifestation of symptoms. Owing to these facts, naturally, the first symptoms of a rectosigmoidal cancer are frequently those indicative of a partial obstruction. Sometimes patients with malignant growths in this region first consult a physician because of an acute obstruction. Neoplasms of the rectal ampulla, owing to the large size of the lumen, rarely cause marked obstruction and then only after the lesion is far advanced. Cellular, fungoid growths which are prone to early ulceration and bleeding are the type of tumors often seen here and in the lower part of the rectum. Blood and mucus in the stools are the usual first signs of a malignant condition of this part. Cancers of the anus are usually epitheliomas. They early become fissured, ulcerated and infected. Because of this and the resulting spasm and contraction of the sphincter muscles, a discomfort or even pain is frequently and early a manifestation of neoplasms of this location. The position of the carcinoma will also have a direct bearing on its accessibility and therefore the type of operation to be performed and the hazard of its removal. So the location of the lesion has a definite relation to the pathologic condition, the symptoms, the treatment and the prognosis.

Improper first treatment is a definite factor affecting the cure of rectal cancer. Many patients are treated for hemorrhoids, some being given ointments even without an examination. Occasionally the patient is treated for colitis. Sometimes an injection is made into a malignant lesion, and for others a local cauterization is done. A review of the records of these 167 cases referable to the nature of recent treatments before admission to the hospital shows that fifteen patients had a hemorrhoidectomy performed, nine were given injections for hemorrhoids, five had a local cauterization of the lesion, ten other patients had some other type of surgical work, and twenty-seven had some kind of medical treatment. It is seen by this review that sixty-six patients, or approximately 40 per cent, had some type of inadequate therapy before their conditions were definitely diagnosed. Most patients, previously subjected to either injections or local cauterization before having wide removal of the neoplasm performed, have not remained well. Incomplete operations unquestionably do harm by tending to disseminate the disease and by preventing the patient from coming earlier for proper treatment.

22. Buie, L. A., and Bargen, J. A.: Malignant Anal Lesions of Epithelial Origin, Journal-Lancet **53**: 565 (Nov. 1) 1933.
23. Newman, George: Great Britain Ministry of Health Report on Public Health and Medical Subjects, London Bulletin 46, 1927.
24. Yeomans, F. C.: Perineal Excision of Cancer of Rectum, Am. J. Surg. **27**: 226-230 (Feb.) 1935.
25. Mechling, C. C.: Cancer of the Rectum, West Virgina M. J. **31**: 57-59 (Feb.) 1935.

The attitude of some physicians occasionally is discouraging. They assume that treatment is of no avail and therefore that all cases of rectal cancer are hopeless. While it is true that many of these patients come to the physician with lesions so advanced as to be irremovable, there are, on the other hand, more than 50 per cent of the patients for whom the growth can be removed with a definite prolongation of life for some, and for many others a permanent cure. As stated previously, twenty-two patients declined surgery and of the 145 remaining patients of this series the cancerous intestine was removed for seventy-six, or 52.4 per cent.

TABLE 1.—*Type of Operation with Results*

	Number	Hospital Deaths
Anterior excisions with colostomy	6	—
Anterior resections without colostomy	2	—
Combined excisions	9	2
Posterior hot-knife excisions with colostomy	48	1
Posterior hot-knife excisions without colostomy	5	—
Local cautery excision of early lesions	5	—
Fulguration malignant papilloma	1	—
Total	76	3
Per cent		3.9

If the twenty-two patients declining had accepted surgery, the percentage of operability would have been materially increased.

The type and thoroughness of the operation performed are two of the most important factors influencing the curability of this disease. The combined abdominoperineal excision is the anatomically correct and classic operation; but to adopt it as a routine method has not seemed wise. Rankin [26] writes that he has found the operation as advocated by Miles not to be applicable for more than 20 per cent of these cases. Reporting on another group of patients, he states that less than one third were considered suitable for this type of excision. Wilkie states that the Miles operation presents difficulties and risks that are serious and unjustifiable in approximately 50 per cent of the cases. The combined operation certainly entails a greater surgical hazard. Dixon believes that the average mortality for the combined procedure is about 12 per cent and reports only 4 per cent for the posterior excision. Unquestionably rectal neoplasms should not and cannot all be operated on by the same surgical plan. A graded operation, with the procedure divided into two or more stages, is usually preferable, doing much to lower the surgical mortality. Occasionally a rectosigmoidal lesion can be removed by an abdominal approach. A majority of lesions in the rectosigmoid and upper part of the rectum, however, should have a combined abdominoperineal excision, usually in two stages. Some neoplasms of the ampulla are preferably removed by the combined method, but for a majority of tumors of the ampulla and for most cancers of the lower part of the rectum and anus a posterior hot-knife excision, following a preliminary colostomy, seems preferable.

Radiation therapy deserves proper consideration. Five year cures by this method of treatment have been reported by several, among whom are Bowing, Binkley [27] and Gordon-Watson. While my experience has been limited, I would reserve this therapy primarily for the treatment of the patients with inoperable neoplasms, for those whose physical status will not permit surgery, for the patients who refuse to accept surgical treatment, for grade 4 malignant growths, for the extensive anal epitheliomas and as an adjunct to surgery. Practically all patients treated surgically were given either preoperative or postoperative irradiation, and some were given both.

The instrument used by the surgeon for the excision may be a definite factor affecting the end result. The use of the hot-knife for the removal of a cancerous rectum has much to commend it. The hot-knife is a sharp, platinum, loop cautery tip, heated electrically. The advantage gained by the general adoption of the hot-knife for the excision of carcinomatous tissue has been stressed repeatedly by my senior associate, A. C. Scott.[28] My further experience with the cautery confirms conclusions published in a previous paper.[29] I find that the difficulty of the excision is not augmented by the use of the cautery knife. A line of cleavage is more readily obtained by it and therefore a more accurate dissection can be made. Larger and more advanced growths can be removed with the hot-knife, thereby extending the field of operability. The lymphatics are sealed when severed, and therefore there is less likelihood of dissemination of the cancer cells. There is diminished absorption of toxic substances from the wound, since the lymphatics are sealed. The loss of blood is less, for the hot-knife tends to close the capillary and small blood vessels. The postoperative pain is decreased. Because of these facts, the frequency and degree of shock are lessened and recurrence is definitely diminished.

In our clinic we have performed forty-eight consecutive posterior hot-knife excisions of malignant rectums with only one operative death, or a mortality of approximately 2 per cent. This fact would seem to justify the statement that it is a safer procedure than the usual knife excision. A surgical removal of the cancerous rectum by some method was performed for seventy-six patients. There were two other hospital deaths, or an operative mortality for the entire surgical group of 3.9 per cent. The fact, which is substantiated by these statistics, that the surgical extirpation of a malignant rectum is a relatively safe procedure with a low mortality should be emphasized, in the hope thereby that patients will earlier and more readily accept treatment.

TABLE 2.—*Glandular Metastasis Affecting Curability in Fifty Resected Specimens from Patients Operated on More Than Three Years Ago*

		Good Results		Poor Results	
	Number	Number	Per Cent	Number	Per Cent
Patients without glands involved	40	27	67	13	33
Patients with glands involved	10	3	30	7	70

A detailed study has been made of fifty resected rectal carcinomas from patients operated on more than three years ago. The accompanying tables give an analysis of the work. Forty-eight patients were operated on five years or more ago. There were two hospital deaths, and two cases have not been traced.

26. Rankin, F. W.: Two Stage Resection for Carcinoma of the Rectosigmoid and Rectum, Surg., Gynec. & Obst. **53**: 670 (Nov.) 1931; A Survey of the Treatment of Carcinoma of the Rectum and Rectosigmoid, Interstate Postgraduate Assembly, North America, October 1932.

27. Binkley, G. E.: Gold Radon Seeds in Rectal Cancer, Ann. Surg. **102**: 72 (July) 1935.

28. Scott, A. C.: An Evaluation of Agents That Destroy or Remove Malignant Disease, J. A. M. A. **97**: 385 (Aug. 8) 1931.

29. Brindley, G. V.: Cancer of the Rectum, Study of One Hundred Case Records, South. M. J. **25**: 441-448 (May) 1932.

Twenty-two patients, or 50 per cent, of the remaining forty-four obtained from five to fourteen years of good end results from surgical treatment. Thirty-three of these forty-eight patients were operated on by the method of posterior cautery excision after a preliminary colostomy had been performed. The two untraced patients were in this group and two other patients are known to have died from some cause other than a recurrence of the malignant condition. Of the remaining twenty-nine, fourteen, or 48 per cent, obtained five years or more of good end results. Therefore the ultimate results obtained by a posterior hot-knife excision further commend its adoption for the extirpation of a rectal cancer.

TABLE 3.—*Degree of Malignancy Referable to Clinical Types*

Pathologic Report	Number Graded	Grade 1	Grade 2	Grade 3	Grade 4
Papillary adenocarcinoma	26	7	11	8	..
Adenocarcinoma	84	2	42	35	5
Colloid carcinoma	4	..	1	3	..
Total	114	9	54	46	5
Per cent		7.66	47.4	40.6	4.33

TABLE 4.—*Extent of Lesions Affecting Curability: in Fifty Resected Specimens from Patients Operated on More Than Three Years Ago*

	Number	Good Results	Per Cent	Poor Results	Per Cent
Lesions confined to mucosa	21	18	85.7	3	14.3
Invasion of muscle wall	4	3	75	1	25
Penetration to or beyond serosa	25	10	40	15	60

TABLE 5.—*Grade of the Malignancy Affecting Curability in Fifty Resected Specimens from Patients Operated on More Than Three Years Ago*

	Number	Good Results	Per Cent	Poor Results	Per Cent
Grade 1	3	3	100	0	....
Grade 2	26	16	61.5	10	38.5
Grade 3	19	11	57.9	8	42.1
Grade 4	2	0	....	2	100

CONCLUSIONS

Carcinoma of the rectum is a curable disease. Many factors influence the treatment and prognosis of the patient with a cancer of the rectum, making it wise to study and treat each case individually. Among these factors are to be considered the location, the size and the extent of the lesion, the mobility of the growth, the pathology of the neoplasm, the sex, age, physical state and attitude of the patient, the availability of radium and roentgen therapy, proper preoperative and postoperative care of the patient, and the instrument used for the excision of the malignant intestine. The salient facts to be remembered are that cancer of the rectum is a local lesion for a few months; that the spread of carcinoma here tends to be slow; that the first symptoms are a change in the frequency and character of stool; that the diagnosis can be made easily, early, with certainty by simple measures; that the rectum is not a vital organ; that a colostomy is not particularly disabling; that the surgical removal of a malignant rectum is a relatively safe procedure, and that wide, hot-knife excision of early lesions gives a high percentage of permanent cures.

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ABSTRACT OF DISCUSSION

DR. CURTICE ROSSER, Dallas, Texas: A few years ago biopsy enjoyed an entirely undeserved oblivion. Partly because it has been found that "examination-massage" of a malignant tumor is probably as dangerous as or even more dangerous than the careful removal of a section of that tumor, and partly because of the perfection of instruments for biopsy, including the use of the coagulating current, biopsy is now a more or less standard procedure. In spite of the fact that a great many more physicians are now equipped by experience to recognize a typical malignant growth of the rectum by inspection and palpation, there continues to be a need for microscopic tissue examination. The statistics of Dr. Brindley have shown that a person with a grade 4 malignant growth of the large bowel will probably die of cancer eventually, regardless of what is done about it, and a biopsy in that instance might change one's plan of attack on the growth. At the other extreme, a person with a grade 1 cancer may survive after even a simple local removal; consequently, the advance information afforded by biopsy has definite value here. Frank recognition of the etiologic significance of benign lesions of the rectum and anus in relation to rectal cancer will do a great deal to advance the time at which a definite diagnosis can be made. That adenoma of the rectum is a direct etiologic factor is now generally conceded. I reported before this section in 1930 a group of cases of long standing, inflammatory and irritative lesions of the anal canal, such as hemorrhoids, fistulas and anal ulcers in which there was definite evidence that the benign lesions had an etiologic significance in connection with the malignant growth that was discovered superimposed. A mixed tumor of this type—an implanted malignant growth on the basis of an adenoma or an old inflammatory lesion of the anal canal—frequently fails to give a clear-cut picture on examination through the proctoscope. A biopsy is therefore advisable when the suspicion of malignancy is aroused. Accurate and comprehensive diagnostic measures are essential in the presence or possibility of any rectal neoplasm. The entirely laudable attempt to popularize rectal examinations on the part of the practitioner has at the same time deeply inculcated the idea that this procedure may properly consist entirely of the casual introduction of the index finger. The fact that the majority of rectal tumors in their curable stages are in the upper rectal zones suggests that careful direct visualization of the entire rectum and rectosigmoid is likewise indicated. The fortunate trend of opinion that has rescued biopsy from its previous disfavor affords an additional safeguard to the patient when the presence of a malignant condition or the degree of malignancy is undetermined.

DR. FRED W. RANKIN, Lexington, Ky.: I disagree with Dr. Brindley on one point. I have the firm conviction that the most important factor influencing prognosis is the activity of the cancer cell as graded by Broders' classification of malignancy, and I believe firmly that these other factors of duration of growth, glandular metastasis and the extension of the malignant process through the muscularis of the bowel and into the regional lymphatics, and beyond, are in direct ratio to this activity. Broders has shown very clearly just what Dr. Brindley's experience has been here, that the cancer of the rectum has a tendency to occur most often in the lower grades, 1 and 2. My figures were 65 per cent in the grade 1 and grade 2, and I think that this accounts in large measure for the hopeful prognosis following the successful extirpation of cancers in this region. Let me also emphasize the fact that in resected specimens of cancer of the rectum 46 per cent show glandular involvement. I believe that when possible radical surgery should be applied after the principles of Halstead not only to the breast, the lip, the tongue and the stomach, but also to cancers of the rectum. I heartily agree with Miles's statement that it is just as important to remove the mesentery of the sigmoid in doing a radical operation for cancer of the rectum as it is to remove the glands of the axilla in doing an operation for cancer of the breast. Within the last three years I have found myself changing more and more from the graded procedure of my own, which is a modification of Miles's operation, and somewhat similar to Lahey's modification, brought out in 1929, to the one-stage operation of Miles. In a high percentage of cases, however, debilitated and desiccated individuals are seen too late to apply this radical procedure in a

routine manner and for that reason it is necessary to resort to the less radical procedure of colostomy and posterior resection. In the last fifty cases I did eighteen one-stage operations, sixteen colostomies and posterior resections, and four of my own type of operations. In that group of resections, one patient died following resection and colostomy and eighteen survived radical one-stage operations but I don't think that is a fair way to estimate operative mortality, for, in the whole fifty, actually five patients died, four of them following colostomy alone.

DR. G. V. BRINDLEY, Temple, Texas: I wish to express appreciation to Dr. Rosser and Dr. Rankin for the manner in which they amplified the paper in their discussions. Unquestionably rectal neoplasms should not all be operated on by the same surgical plan. It was shown on the screen that I use six different types of operation. The location of the growth, the age of the patient, the degree of malignancy, the extent of the lesion and the patient's physical status are all very important factors in determining the type of operation to be performed. The hazard of the different procedures must be weighed in making the selection. It is generally accepted that a combined excision carries a mortality of about 12 per cent, contrasting with the 4 per cent mortality of a posterior excision.

Clinical Notes, Suggestions and New Instruments

QUININE TREATMENT OF MYOTONIA CONGENITA

WILLIAM A. SMITH, M.D., ATLANTA, GA.

Wolf [1] has recently reported striking benefit obtained by the use of quinine in four cases of myotonia and has concluded that quinine is a specific for this disorder, which has shown practically no response to all previous methods of therapy. I have had an opportunity to confirm this remarkable discovery in three cases, which will be briefly reported.

The familial disease known as myotonia congenita was first described in 1876 by Thomsen, a Danish physician. He himself and twenty members of his family were affected. The disease is characterized by tonic muscular spasms occurring at the start of a movement, which greatly restrict further action. With repeated attempts at movement the spasms relax and the movement gradually becomes more free, until there is no difficulty. After a period of inactivity, however, the spasm occurs on attempted activity. The condition is usually worse when the patient is cold or fatigued. Such tonic spasms, with marked delay in relaxation, occur not only on voluntary movement but also with mechanical or electrical stimulation, and even on reflex contraction such as coughing or sneezing. The skeletal muscles are often greatly overdeveloped, although muscular power may be diminished. The disorder may be generalized or limited to certain muscles. Symptoms usually begin in childhood but sometimes do not appear until puberty or later.

The disease causes considerable disability as well as great embarrassment. On arising from a chair there may be spasms in the legs and inability to move, the patient sometimes falling forward on his face. On attempting to walk fast or run, similar spasms prevent movement until relaxation occurs. Ascending stairs is especially difficult. In shaking hands, the patient often has difficulty in releasing the hand grip. In starting to speak, spasm of the tongue and lips may prevent speech for a few moments. It attempting to chew, spasm of the jaw muscles makes this very difficult at first. Even the ocular muscles may be involved. Neurologic examination usually gives normal results except for the hypertrophied muscles, the tonic spasms on movement and the slow relaxation following contraction.

The etiology is obscure. The condition simulates that produced by veratrine poisoning. By electromyographic studies, Lindsley and Curren [2] have shown that the spasm is a reflex phenomenon, which they thought due to abnormal irritability of sensory organs in the muscles. Throughout the years no effective remedy has been known, although numerous methods of therapy have been tried.

The effect of quinine in the following cases has been very gratifying:

A white youth, aged 19 years, seen in November 1934, complained of difficulty of rapid movement, which had been present as long as he could remember; whenever he stopped moving, it would be difficult to get started again because of a muscular spasm. When first attempting to walk or run, his legs would become very stiff, which sometimes caused him to fall. In getting up from a chair, his knees would suddenly lock, and he would have to wait for them to relax before being able to move. He had noticed the same difficulty on use of the arms and had difficulty in releasing his hand grip. Later, similar disorders appeared in the muscles of the jaw and tongue with difficulty in starting to chew or to speak. By slowly "warming up" he would be able to continue these movements without difficulty. While attempting to drill in college, he was unable to keep up with the other boys, as whenever they stopped he would be unable to start marching again on command. He had had large muscles since childhood.

The examination showed enlargement of practically all the skeletal muscles. There were tonic spasms on sudden movements, most marked in the extremities. A myotonic reaction with marked delay in relaxation was also present on mechanical and electrical stimulation of the muscles. There were no other significant abnormalities. A diagnosis of myotonia congenita was made.

Sept. 27, 1936, he was given an intravenous injection of quinine dihydrochloride 7½ grains (0.5 Gm.) and in thirty minutes there was practically complete disappearance of all myotonic symptoms, including the myotonic reaction on electrical stimulation. The oral administration of 7½ grains twice daily has been found to be sufficient to maintain freedom from symptoms.

Two sisters, aged 17 and 8 years, had noticed similar though milder symptoms for several years. Both have obtained relief by the oral use of 5 grains (0.3 Gm.) of quinine daily.

CONCLUSION

The value of quinine in myotonia congenita has been confirmed in three cases.

911 Medical Arts Building.

1. Wolf, Alexander: Quinine: An Effective Form of Treatment for Myotonia; Preliminary Report of Four Cases, Arch. Neurol. & Psychiat. **36**: 382 (Aug.) 1936.
2. Lindsley, D. B., and Curren, E. C.: An Electromyographic Study of Myotonia, Arch. Neurol. & Psychiat. **35**: 253 (Feb.) 1936.

OPERATION FOR VOLVULUS WITH RECOVERY

BENJAMIN BOROW, M.D., AND HENRY BOROW, M.D.
BOUND BROOK, N. J.

When one considers the embryology of the alimentary canal, it is surprising that anomalies of the intestinal rotation are not more common; probably they do occur oftener than they are recorded, owing to the fact that symptoms are absent. Out of a total of forty-eight cases reviewed by Dott, thirty-five were accidentally discovered, as misplacement did not give rise to symptoms or diagnosis was made late.

The case about to be reported is the first, we believe, in which operation was successfully performed when the patient was 4 days old. To understand clearly the condition to be described, the embryologic course will be discussed briefly in the embryo from the fifth week. At this time the canal consists mainly of three parts, foregut, midgut and hindgut, and all are attached by the common dorsal mysentery. The distal portion of the foregut forms the stomach and duodenum. From the midgut, the small intestine and remainder of the tube are formed. From the hindgut, the descending and sigmoid parts of the colon, the rectum and the tubular diverticulum of the allantois are formed. The midgut has a ventral attachment by the vitello-intestinal duct to the yolk sac, which is lost by the fourth week and, as the midgut grows, it is extended into the root of the cord as a temporary umbilical hernia. Rotation of the gut begins about the fifth week while it is in this position, the next stage occurring at about the tenth week. Because of the bulky hernial content, it is impossible for it to return through the narrow umbilical orifice *en masse*. The ileum is forced out, followed by the colon; as the colon elongates, the cecum descends into the right loin. This stage is anticlockwise and turns about the axis of the superior mesenteric artery of 270 degrees from the premature sagittal position of the loop.

The third stage begins about the eleventh week and progresses until birth or a short time after it, being characterized by further descent of the cecum and fixation to the postabdominal wall of certain parts of the intestine, which reaches its normal position at about the fifth month. The importance of this stage is not so much the degree of rotation as the fixation of parts in such a way that displacement, and especially torsion and volvulus, are rendered impossible. The ileocecal angle thus is held steady by adhesion of the cecum and ascending colon.

The only derangement taking place during the first stage of rotation is extroversion of the cloaca, which includes the opening of the ureters, genital ducts and intestinal canal. The derangements occurring during the second stage may be a nonrotation of the midgut loop, a reversed rotation or a malrotation of the midgut loop. These, Dott believes, are due to the variation in size of the embryonic umbilical orifice. The third stage of rotation maladjustment would be due to early or delayed fixation of the cecum, the former causing an undescended cecum, the latter an overdescended cecum.

The type of obstruction in this case was a volvulus. The predisposing causes were a narrow base to the loop of intestine, an undue length of mesentery and a point of adhesion at the convexity of the loop, which can act as an axis of rotation. The exciting cause was a peristaltic motility or undue distention of intestine.

REPORT OF CASE

J. H., the first child of young parents, was born Sept. 19, 1935. Delivery was normal. The child weighed 6 pounds 13 ounces (3,090 Gm.) and passed meconium from the bowels on the first day. On the second day it passed mucus and about two drops of bright red blood. Rectal irrigations and glycerin and oil enemas were given. The result was a very small amount of flatus.

Physical examination was negative until the fourth day, when some distention was present. On the fourth day a duodenal tube was placed in the stomach and about one-half ounce (15 cc.) of thick viscid bile was withdrawn. Roentgenograms showed a diverticulum of the esophagus and obstruction in the ileum.

Drs. Lathrop and Donovan were called in consultation. The objections of the father and family to operation delayed matters for eight hours. In the meantime the baby's temperature rose from 99 to 103 F. and, during the day, emesis was yellowish green. The infant received 5 per cent dextrose in saline solution previous to the operation and afterward.

The child was operated on under local anesthesia, supplemented by ether. A right paramedian incision was made, the wall being almost one-eighth inch in thickness. Considerable amount of yellowish fluid appeared. The ileum was edematous. There was marked distention of the stomach and upper intestine. The mesentery was markedly indurated, and hemorrhagic areas were present. There was a twist in the longitudinal axis of 360 degrees in a clockwise direction. Above the constriction the intestine was dilated to about the diameter of 1½ inches, while below it was constricted to about three-eighths inch. The twist was reduced by rotating the whole mass in the anticlockwise direction and the intestine was returned into as normal a position as possible with considerable difficulty owing to the amount of distention present. The abdomen was sutured in layers and closed without drainage.

Blood transfusion of 20 cc. of the father's blood was given after the operation and repeated the following day; continuous clysis of saline solution and 5 per cent dextrose was also given. Breast milk given after operation was not retained. Lavage was done, returning fecal-like material. Irrigations and stupes were ordered. Enemas of milk and molasses were given. One minim (0.06 cc.) of solution of posterior pituitary was given on the second day. Lavages were done every two to four hours for three days, as the stomach filled with fecal-like material. On the third postoperative day rectal irrigation returned brownish, with a few fecal particles. After the bowels started to move, the baby was able to hold breast milk by mouth in which 5 drops of whisky was added. Diarrhea followed, which was finally controlled by banana powder. One week following the operation the baby weighed 5 pounds 8 ounces (2,495 Gm.) and continued to gain weight slowly. The general condition has been good and at 1 year of age the child weighed 19 pounds 4 ounces (8,730 Gm.).

507 Church Street.

Special Article

THE PHARMACOPEIA AND THE PHYSICIAN

DRUG TREATMENT OF CARDIAC DECOMPENSATION

HENRY A. CHRISTIAN, M.D.
BOSTON

This is one of a series of articles written by eminent clinicians for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopeial Committee of Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.

By cardiac decompensation is meant a combination of symptoms and signs that indicate that the heart by reason of its abnormal condition no longer is able to maintain an efficient circulation. In cardiac decompensation is not included the circulatory failure of acute infectious diseases. Various forms of heart disease may lead to the condition spoken of as cardiac decompensation, such as chronic valvular heart disease, chronic nonvalvular or myocardial heart disease, chronic pericarditis or congenital cardiac lesions. As factors in the production of these forms of heart disease, rheumatic fever and hypertension play very important rôles, the former being the causative factor in almost all the chronic lesions of valves and the pericardium, the latter with arteriosclerosis of the coronary arteries, thyroid disease and possibly the effects of infections being the usual causative factors in the myocardial group. Syphilis of the aorta with aortic insufficiency is the cause of cardiac decompensation in a special group, while the same disease has a definite but quantitatively uncertain, probably slight, part in producing myocardial disease.

In the presence of these cardiac lesions in due course of time will appear the symptoms and signs of cardiac decompensation, of which the most important are breathlessness, cough, edema and cardiac enlargement. As a rule, a correct diagnosis of cardiac decompensation is made easily; not infrequently, however, the etiology in a given case cannot be recognized with certainty. Fortunately, in most patients with cardiac decompensation recognition of the exact etiology plays little part in methods of treatment; the chief exceptions to this are syphilis and thyroid disease, and here the use of the Wassermann reaction and determinations of basal metabolism along with other evidence give quite a clear clue to these relationships of etiology utilizable in treatment.

Given then any of these conditions with resultant cardiac decompensation sufficiently marked to incommode the patient greatly, certain therapeutic procedures are indicated for each patient. Such a patient needs primarily physical rest; with few exceptions this should be bed rest with the patient comfortably propped in a half sitting posture; in a small number of cases a chair position is required for the first few days.

Since many cardiac patients have been prevented by their symptoms from getting sufficient sleep, a very important part of the early treatment is to give a drug that will produce a good night's rest; for this purpose hypodermic injection of morphine sulfate, from one-sixth to one-four grain (10 to 15 mg.), is most effective, and this can be repeated for a night or two until

other therapeutic measures have so improved the circulation that the patient will sleep satisfactorily without any further sedation.

The drug of greatest value in the treatment of cardiac decompensation is digitalis. With extremely few exceptions digitalis is effective when given by mouth, and no form is superior for mouth dosage to the very simplest form of the drug, pills or capsules of powdered digitalis leaves. For patients with marked decompensation not having received digitalis in any form within the past week the initial dose should be 7½ grains (0.5 Gm.) to be repeated in four hours and usually again four hours later, the patient thus receiving 22½ grains (1.5 Gm.) in the first eight hour period. After this, 3 grains (0.2 Gm.) or 1½ grains (0.1 Gm.) three times a day should be given and continued until a therapeutic effect or some evidences of toxicity result. The original directions of William Withering in 1783 as to giving digitalis cannot be improved on: "Let the medicine be continued until it either acts on the kidneys, the stomach, the pulse or the bowels; let it be stopped upon the first appearance of any one of these effects."

Tincture of digitalis may be substituted in mouth dosage for the powdered leaves if for any reason that seems desirable; rarely, however, in my experience is that the case; if for no other reason, the convenience of pills and capsules would give a preference to powdered leaves over the tincture; however, it has always seemed to me that the whole leaf has a therapeutic superiority to the alcohol soluble portions present in the tincture.

The foregoing dosage should be increased for cases of greater severity and for very large patients. Conversely, for patients with less marked degree of cardiac decompensation and for small patients the initial large doses may be curtailed or abandoned. This abandonment of the large initial doses particularly is indicated when the patient previously has been getting digitalis in any considerable dosage.

In all of these statements of dosage, it is assumed that all preparations of digitalis are of standard Pharmacopeial activity as determined by the biologic test contained in U. S. P. XI.

For patients extremely ill, in whom a digitalis effect must be prompt to save life, intravenous medication is indicated. For this, strophanthin or ouabain is best, the intravenous dosage being from 0.5 to 1 mg., not to be repeated within twenty-four hours and not to be used in a patient recently having received previously digitalis in other form in other than very small dosage. Extremely few patients need this intravenous form of therapy.

In some patients in whom nausea and vomiting prevent mouth dosage, strophanthin or ouabain, as described, can be used until the gastric symptoms subside sufficiently to permit a return to mouth dosage. In this type of patient, instead of strophanthin or ouabain intravenously, tincture of digitalis can be given by rectum in a dosage of 1 or 2 drachms (5 to 10 cc.) once or twice daily, followed by a small amount of physiologic solution of sodium chloride, the injection being preceded by a bland cleansing enema.

At present there is no advantage to be obtained by using any other than Pharmacopeial preparations of digitalis, notwithstanding the many proprietary digitalis preparations that are being offered with great enthusiasm to the medical profession, their dispensers making many claims for their superiority, claims that seem not justified as far as my own clinical experience goes.

In some patients with cardiac decompensation, edema is marked. Often it disappears rapidly as the result of the digitalis and rest therapy. When it does not, diuretic drugs are indicated. For mouth dosage one of the xanthin group can be used, as theobromine with sodium salicylate, theophylline or theophylline with sodium acetate. These should be given in two or three doses at two hour intervals every second or third day, the first dose being given early in the morning, the single dose of the theobromine group being from 7½ to 15 grains (0.5 to 1 Gm.) and of the theophylline group from 5 to 7½ grains (0.3 to 0.5 Gm.).

In case the xanthin group of diuretics are not sufficiently effective, the mercurial diuretics such as merbaphen (novasurol) should be utilized, for they are more effective as diuretics than are the xanthin group. However, they are not effective by mouth dosage but must be given parenterally, preferably intravenously, though they may be given intramuscularly with risk of some local irritation. These mercurials are prepared in ampules ready for parenteral dosage as a 10 per cent solution of the drug. The dose of this preparation is from 1 to 2 cc. by either route at two or three day intervals. Like the xanthin diuretics, they should be given early in the morning, so that the major diuresis ends before bedtime. Of the mercurial diuretics, salyrgan and mercupurin, not so far included in the Pharmacopeia, definitely are less toxic and more effective than merbaphen and so are preferable. At present there are available mercurial preparations of salyrgan and the mercurial portion of mercupurin, which are effective by rectum in the form of a suppository; the availability of these at times is a great help in the management of edematous cardiac patients.

To obtain the best effects from mercurial diuretics, often ammonium chloride or ammonium nitrate needs to be given for from twenty-four to forty-eight hours prior to using the diuretic in doses of 15 grains (1 Gm.) four times a day. These drugs should be given well diluted with water or fruit juice or in the form of tablets, coated so as to prevent solution by the gastric juice.

When there is hydrothorax present, this should be removed in the beginning of the treatment by tapping. It is inadvisable to attempt to treat this situation by diuretic drugs. Ascites usually disappears under diuretic therapy, as just described; failing to do so, mechanical removal is indicated.

In patients of this group in whom coronary circulation is defective, it is believed by some that improvement in the rate of coronary flow with resultant dilatation of the collateral vascular channels and eventual improvement in myocardial function can be brought about by the use of theophylline with ethylenediamine in doses of 1½ grains (0.1 Gm.) three times a day, the drug diluted in half a glass of water to decrease gastric irritation. I myself remain unconvinced of any great effectiveness from this drug for this purpose.

In a rare patient with cardiac decompensation having auricular fibrillation in whom digitalis fails to bring about improvement, betterment may come from making the cardiac rhythm regular by the use of quinidine sulfate. To accomplish this, after a test of quinine susceptibility by a dose of 3 grains (0.2 Gm.) of the drug, quinidine sulfate then should be given every four hours in a dose of 6 grains (0.4 Gm.) until rhythm becomes regular, or even larger dosage may be used. However, it is well to remember that to carry out such treatment has a certain definite, though small, risk, as fatalities

may follow quinidine sulfate dosage. If a patient receiving quinidine sulfate shows signs of collapse, caffeine in some of its forms (caffeine, citrated caffeine, and caffeine with sodium benzoate) should be given at once intravenously in 15 grain (1 Gm.) doses, or, if the pulse has failed, intracardiac injection should be attempted. At the same time artificial respiration should be instituted.

Active catharsis now rarely is instituted for patients with cardiac decompensation. If it is considered desirable, magnesium sulfate or compound jalap powder may be used. Mild catharsis to prevent constipation often is desirable for these patients; some form of cascara (extract of cascara, fluidextract of cascara, aromatic fluidextract of cascara) as a rule is satisfactory for this purpose. This failing, other procedures as advised in the article in this series on cathartics can be followed.

If the cause of the cardiac lesion inducing cardiac decompensation is syphilis, the syphilis should be treated after the cardiac decompensation has been managed in the ways described or before it develops. This is to be done with iodide, mercury and bismuth preparations as described in the article of this series describing the treatment of syphilis. As to the use of arsphenamine in syphilis of the aorta there is difference of opinion; my experience indicates that it is of value and that, if used cautiously, it is safe. Mercury or bismuth compounds should be given first for several doses at weekly or biweekly intervals and then followed by arsphenamine, the first doses of the latter being 0.2 Gm. Later the dose can be increased to 0.3 Gm. and eventually to 0.4 Gm. if there are no untoward reactions, the arsphenamine being given once or twice a week. When pain is present as a symptom of syphilitic disease of the aorta, treating the syphilis, as just described, often is very beneficial as concerns that symptom. Statistics seem to indicate that such treatment of the syphilis has practically no influence on cardiac decompensation but that it may slow the progression of the syphilitic lesion and so prolong life. Antisyphilitic treatment should be instituted as soon as the lesion is diagnosed, preferably before cardiac decompensation is in evidence. Those with experience with syphilis of the myocardium generally advise against arsphenamine but use the other antisyphilitic drugs in its treatment.

When hyperthyroidism is a causative factor in cardiac decompensation, proper surgical treatment of the thyroid should be carried out as soon as cardiac decompensation has been controlled sufficiently to make subtotal thyroidectomy reasonably safe. The results are very satisfactory.

With the form of cardiac disease due to thyroid deficiency or myxedema, striking improvement promptly follows properly adjusted mouth dosage of thyroid gland substance. Care must be taken, however, not to give it so as to restore too rapidly the thyroid deficiency, since in so doing one may place too great a burden on the heart and produce symptoms in this way, especially anginal pain. It is well to begin with a dosage not greater than one-fourth grain (15 mg.) of a thyroid gland preparation standardized as to efficiency by the method described in the Pharmacopeia. Determinations of the rate of basal metabolism serve as an effective guide to treatment in these patients.

During the early stages of treatment of cardiac decompensation, diet should be limited to small amounts of milk, from 800 to 1,000 cc. daily. After a few days, carbohydrate and egg should be added. Later a more liberal diet based on the caloric requirements of the patient should be given. Frequent small feedings are indicated so long as decompensation persists. Fluid intake in these patients should be restricted to from 1,200 to 1,500 cc. As many of these patients are overweight, the diet should be gaged so as to bring about proper reduction in weight until the patient that has been overweight is from 10 to 15 pounds (4.5 to 7 Kg.) underweight; but this reduction must be carried out slowly. The diet must be adequate in constitution to prevent vitamin deficiency. Many cardiac patients need added vitamin in their diet, and some of these may be supplied by using properly standardized preparations as well as by giving diet adequate with respect to them.

Practically all patients with cardiac decompensation, after that has been treated satisfactorily, need to continue to take digitalis indefinitely in amounts just short of causing toxic disturbances. For the majority of patients this is 1½ grains (0.1 Gm.) of powdered leaves, once or twice daily; a few patients do better on either more or less than this, as determined by trial.

Peter Bent Brigham Hospital.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

TETRACHLORETHYLENE.—". . . contains not less than 99 per cent and not more than 99.5 per cent of $CCl_2:CCl_2$, the remainder consisting of alcohol." *N. F.*

For standards see the National Formulary under Tetrachlorethylenum.

Actions and Uses.—Observations of many workers have shown that tetrachlorethylene is a useful anthelmintic for the treatment of hookworm infestation. It has been used against other worms with less success, although there is some evidence that it is useful in Trichuris infestation. It may be lethal to Ascaris but its use in that infestation is not advised because of the danger of causing migration of the worms. It is the consensus of the investigators that tetrachlorethylene is less toxic than carbon tetrachloride (CCl_4) and at least as efficacious as the latter drug. It has a further advantage over carbon tetrachloride in that it does not lower the guanidine content of the blood, which is important in cases exhibiting a calcium deficiency. Untoward reactions are rare, but giddiness, vomiting and drowsiness have been reported in some cases. It is probably better to keep the patient (especially children) in bed during the treatment.

Dosage.—From 1 to 3 cc., depending on the age of the patient. Tetrachlorethylene is usually given in soft gelatin capsules but has also been administered to children on a lump of sugar. The gastro-intestinal tract should be thoroughly emptied before administering tetrachlorethylene. Fats and alcohol must be avoided, because they favor absorption of the drug. A dose of tetrachlorethylene should be followed by a saline cathartic of sodium or magnesium sulfate. One dose frequently suffices, but if necessary it may be repeated once after a period of from ten days to two weeks.

NOTE.—Broken capsules should be discarded; the solution should never be employed if it has been exposed to the air for more than a very brief time, because of the possibility of phosgene formation by decomposition.

Tetrachlorethylene-Calco.—A brand of tetrachlorethylene N. F., marketed in soft gelatin capsules each containing 1 cc. of tetrachlorethylene.

Manufactured by Calco Chemical Co., Inc. (a division of the American Cyanamid Co.), Bound Brook, N. J. No U. S. patent or trademark.

Tetrachlorethylene-Calco, 1 cc.

Council on Foods

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

FRANKLIN C. BING, Secretary.

LAMBERT'S V. M. C. AND V. M P. NOT ELIGIBLE FOR THE LIST OF ACCEPTED FOODS

The W. H. Lambert Laboratory of St. Louis presented two products which they call V. M. C. (initials standing for vitamins, minerals, cereals) and V. M. P. (meaning vitamins, minerals, protoplasm) with the request that they be considered by the Council on Foods of the American Medical Association. Proposed advertising copy, descriptions of the products and other information required by the Council were also presented.

The product V. M. C., according to the information which the company has supplied, is a powdered mixture of sugar, cocoa, powdered skim milk, hard winter wheat, malt extract, wheat germ meal, dicalcium phosphate, brewers' yeast, karaya gum, alfalfa leaf meal and salt, flavored with vanillin. V. M. P. is stated to be a powdered mixture of karaya gum, alfalfa leaf meal, dehydrated lemon juice, brewers' yeast, wheat germ, dicalcium phosphate and citric acid. The company later informed the Council that the products have been fortified with a fish liver oil concentrate supplying vitamins A and D. The products are referred to by the company as "special purpose" foods. The Council cannot accept such hodgepodge mixtures for its list of accepted foods.

In the heyday of "patent medicine" interests a nostrum was essentially a mixture of drugs, endowed with a proprietary name, and exploited with unwarranted therapeutic claims. Today the manufacturer of "health foods" puts together a potpourri of alfalfa and other products, adds a little flavoring, and claims that the mixture is not a drug but a food. The composition of such bizarre products is generally predicated on the theory that the diet is deficient in a number of dietary essentials and that, if one mixes together various salts and inexpensive fad products with a little flavoring, it can be foisted on the unfortunate public as a panacea for whatever human imperfections and ailments the clever copy writer cares to mention. The advertising claims rival those made for the alleged virtues of the old-time "patent medicines." The ignorance of nutrition displayed by such promoters is equaled only by the extravagance of their claims.

Could the blatant copy of "patent medicine" concerns have produced anything more fanciful than the statements first proposed for Lambert's V. M. C.:

> "Helps increase weight, aids digestion, stimulates appetite, builds up the blood, improves health and complexion, feeds nerves, benefits teeth, bone development, laxative."?

The claims for V. M. P. are equally extravagant:

> "V. M. P. helps reduce surplus fat in a safe natural way. It improves the complexion, feeds nerves, benefits teeth, bone development, builds up blood, aids digestion and naturally eliminates constipation."

The advertising copy submitted for a proposed booklet describing the products expands on the absurd claims described on the labels. It introduces also amazing dietary advice on how to become beautiful both in face and in figure. The initial heading reads "Have an alluring figure, charm and health." There are many subheadings, such as "The secret of glamorous, attractive women." One is directed how to gain from 15 to 50 pounds in a new, quick, easy way, and, immediately following, how to reduce "ten to thirty pounds safely." The reader is told at the onset that "beauty secrets are between the covers of this book." Further on he is told that the "diet in this one volume tells you exactly how you can be as lovely as the stars if not lovelier."

From information which has more recently come to the attention of the Council, it appears that the label has been revised somewhat. A picture of an artistically posed young woman (unclothed except for a pair of shoes) has been substituted for much of the written material on the submitted label. The inference that the product can create such beauty, however, remains.

The Council on Foods believes the promotion of products such as V. M. C. and V. M. P. portends much harm, particularly because of the false sense of security that may be gained from their inadvised use. The Council voted, therefore, that Lambert's V. M. C. and Lambert's V. M. P. be not included in the list of accepted foods and that the company be informed of this action. This was done and an unsigned communication on the firm's letterhead was received; this was returned for proper signature. No further communication has been received from the firm and the Council has authorized publication of the foregoing report.

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

FRANKLIN C. BING, Secretary.

VIOBIN

Manufacturer.—VioBin Corporation, Chicago.

Description.—Partially defatted and dehydrated wheat germ.

Manufacture.—Commercial wheat germ is extracted by organic solids to remove the fat. The solvent and oil are removed, the defatted wheat germ is treated to volatilize the traces of organic fat solvents, and the product is packed in cans.

Analysis (submitted by manufacturer).—Moisture 7.0%, total solids 93.0%, ash 4.9%, fat (ether extract) 2.1%, protein (N × 6.25) 38.0%, crude fiber 2.9%, carbohydrates other than crude fiber (by difference) 45.1%. Analysis of inorganic constituents showed K 1.08%, Ca 0.067%, Mg 0.353%, P 1.1%, Mn 0.009%, Fe 0.011%.

Calories.—3.6 per gram; 102 per ounce.

Vitamins.—Vitamin B_1, from 14 to 18 units per gram (Sherman Chase), from 7 to 9 units per gram (International).

Claims of Manufacturer.—A special purpose food processed to prevent the possibility of development of rancidity; a rich source of vitamin B_1 and contains vitamin G.

(a) BLISS CRYSTAL WHITE SYRUP
(b) BLISS GOLDEN SYRUP

Packer.—Bliss Syrup and Preserving Co., Kansas City, Mo.

Description.—(a) A table syrup; corn syrup sweetened with sucrose syrup and flavored with vanilla. (b) A table syrup; corn syrup flavored with refiners' syrup.

Manufacture.—(a) Same as Bliss Pancake Crystal White Brand Syrup (THE JOURNAL, Nov. 18, 1933, p. 1635). (b) Same as Bliss Pancake Brand Golden Syrup (THE JOURNAL, Oct. 28, 1933, p. 1393).

Claims of Manufacturer.—Recommended for use as an easily digestible and readily assimilable carbohydrate supplement to milk in infant feeding and as a syrup for cooking, baking and the table.

BELLWOOD BRAND ORANGE JUICE

Distributor.—W. H. Williams Company, Inc., Richmond, Va.

Packer.—TreeSweet Products Company, Los Angeles.

Description.—Heated California Valencia Orange Juice practically equivalent to fresh orange juice in vitamin C content. The same as TreeSweet Pure California Orange Juice (THE JOURNAL, June 15, 1935, p. 2187).

BIG M BRAND HAWAIIAN PINEAPPLE CRUSHED AND SLICED

Distributor.—The Merchants Company, Hattiesburg, Miss.

Packer.—Hawaiian Pineapple Company, Ltd., San Francisco.

Description.—Canned pineapple packed in concentrated pineapple juice with added sucrose. The same as Dole canned pineapple (THE JOURNAL, April 8, 1933, p. 1106).

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JANUARY 2, 1937

CHEMOTHERAPY IN STREPTOCOCCIC INFECTIONS

Since the significant paper of Domagk[1] in 1935, renewed interest has developed in the possibility of chemotherapy in streptococcic diseases. A dark red dye synthesized by Mietzsch and Klarer seemed promising in animal protection experiments. The dye is the hydrochloride of 4′-sulfamido-2:4-diaminoazobenzene. Its toxicity both for mice and for human beings is remarkably slight. In Domagk's report "prontosil," as this dye has been named, was administered by stomach tube to twelve of twenty-six mice an hour and a half after intraperitoneal inoculation with virulent hemolytic streptococci of human origin. All of the twelve that received the dye survived at least seven days. Of the remaining fourteen animals, which served as untreated controls, thirteen were dead within three days and the fourteenth died on the fourth day. Partial corroboration of Domagk's work has been published by Levaditi and Vaisman and considerable suggestive clinical data have been supplied by other German and French investigators. In this issue of THE JOURNAL Long and Bliss[2] indicate the interesting results of their recent investigations at the Johns Hopkins University Hospital.

Colebrook and Kenny[3] have reported other experimental and clinical observations on prontosil and a more soluble modification, the disodium salt of 4′-sulfamidophenyl-2-azo-7-acetylamino-1-hydroxynaphthalene 3:6-disulfonic acid. Their preliminary mouse experiments failed to confirm Domagk's results. When, however, a different streptococcus strain was used which had been transmitted through a series of twenty-three mice and had acquired high virulence for these animals, the results differed from their first experiments. With the latter strain they began at once to get striking curative results in mice when the prontosil soluble was administered subcutaneously or by stomach tube within a few hours after the intraperitoneal injection of streptococci. In fact, the results indicated quite clearly, they believed, that the administration of the drug does exert some curative effect on infections by these hemolytic streptococci in the mouse. The customary evolution to peritonitis and septicemia could be checked in the majority of the animals if treatment was begun within three hours of the injection of the culture. A group of twenty-four mice was tested for the prophylactic effect of prontosil. Of the twelve which received 50 mg. of prontosil subcutaneously before injection of the streptococci, only three died before the seventh day. Of the twelve control mice, nine died before the fourth day. When the surviving animals were subsequently killed, a large deposit of undissolved prontosil was found at the site of injection. It thus seems probable that the prophylactic effect observed was due to slow absorption from this depot. The mode of action of prontosil is obscure. The chief positive facts which emerge from their investigations are that multiplication of streptococci in the peritoneal cavity is prevented if the dye is administered within a few hours. It appears unlikely that the cocci are destroyed either by the drug itself or by some compound formed from it in the animal body. In vitro experiments made with human and rabbit serums disclose no evidence that administration of the drug promotes more active killing of the streptococci by the whole blood. Human leukocytes are but little affected. Apart from the slight growth-retarding influence exhibited by the serum of treated cases there is therefore not much to suggest that either the blood fluids or the blood cells play a predominant part in checking the invasion of the tissues by the streptococci. The hypotheses that the formation of a protective capsule by the streptococcus is interfered with, that the cocci in treated animals ceases to elaborate certain toxic products, that the drug activates the reticulo-endothelial system are all lacking in experimental support.

Buttle and his collaborators[4] have investigated a third related compound, paraaminobenzenesulfonamide base (known commercially as "prontylin") for its protective action in streptococcic infections of mice. The efficacy of a drug for protecting against streptococcic infection can be assessed, they believe, by two criteria: (1) an estimate of the number of average lethal doses of cocci against which the drug will protect when given to infected mice under optimal conditions for action and (2) an estimate of the latest time after infection when its administration will still be operative in saving the animals. The protective action of paraaminobenzenesulfonamide base was tested with six different strains of virulent streptococci. There was a definite difference in the duration and number of survivals between untreated and treated mice, and considerable difference

1. Domagk, Gerhard: Ein Beitrag zur Chemotherapie der bakteriellen Infectionen, Deutsche med. Wchnschr. **61**: 250 (Feb. 15) 1935.

2. Long, P. H., and Bliss, Eleanor A.: Para-Amino-Benzene-Sulfonamide and Its Derivatives, this issue, p. 32.

3. Colebrook, Leonard; Kenny, Meave, and the members of the honorary staff of Queen Charlotte's Hospital: Treatment of Human Puerperal Infections, and of Experimental Infections in Mice, with Prontosil, Lancet **1**: 1279 (June 6) 1936.

4. Buttle, G. A. H.; Gray, W. H., and Stephenson, Dora: Protection of Mice Against Streptococcal and Other Infections by p-Aminobenzenesulfonamide and Related Substances, Lancet **1**: 1286 (June 6) 1936.

in the protection against different strains and in the optimal dosage of the drug. Experiments with staphylococci and pneumococci failed to show any protection. Those with meningococci were uncertain and require further investigation. These observations tend to minimize the likelihood of the dye acting directly and exclusively on the reticulo-endothelial system.

Colebrook and his co-workers also reported briefly on certain clinical experiences with prontosil. Thirty-eight patients with puerperal fever due to hemolytic streptococci were treated by oral and intravenous or intramuscular doses of prontosil and prontosil soluble. The impression was that in many of the more severe cases the drug exerted a definitely beneficial effect manifested by a prompt fall of temperature and remission of symptoms. This was partially corroborated by the death rate, which was 8 per cent in the thirty-eight cases treated, 26.3 per cent in the thirty-eight cases admitted immediately prior to the use of the drug, and between 18 and 28.8 per cent for the four years 1931-1934.

The studies thus far reported abroad on the use of these dyes in the treatment of streptococcic infections are now apparently substantiated to a considerable extent by subsequent investigations. The animal experiments in this country need still further corroboration and there should be efforts to determine the mode of action under different circumstances and in different animals. The clinical observations reported present the usual optimism but there must be adequate clinical controls. Much painstaking effort is necessary before the use of such dyes can be placed on a completely scientific basis. It may be hoped, however, that further investigations will disclose a definite group of disorders characterized by high virulence and mortality which can be materially helped by appropriate chemotherapy.

BRUCELLOSIS

The Brucella group of micro-organisms is commonly divided into Brucella melitensis (the goat strain), Brucella abortus (the bovine strain) and Brucella suis (the porcine strain), all of which may cause brucellosis in man. In a recent review of brucellosis in Iowa, Jordan and Borts[1] point out that infected cows and hogs are the usual source of infection in human brucellosis in that state. With the exception of hogs, which are known to be infected only with the porcine strain, animals may be infected with any of the three closely related types of brucella germs. The symptoms of the disease are weakness, sweating, fever, chills, loss of weight and aching. While treatment at present consists largely in relieving the symptoms of discomfort and the use of medicinal preparations aimed at shortening the duration of illness, some cases have been treated successfully by subcutaneous injections of a Brucella vaccine. During nearly a decade in which the disease has been recognized in Iowa, one or more cases have been reported from all counties in the state. The State Hygienic Laboratories have had a total of about 2,254 positive blood tests during the ten years.

People who live on the farms are more subject to brucellosis than those who live in cities. On the farms the disease affects more farmers than farm wives, because the men come in contact with hogs and cows to a greater extent than do the women. From 1933 to 1935, 319 cases of undulant fever were reported to the Iowa State Department of Health. These have been classified according to residence in rural or urban areas and according to occupation. About half of the number occurred in rural areas, most of which were in male farm workers. In the urban districts the most commonly involved were merchants and professional people, followed by packing house workers, housewives and school children. Of the 318 patients classified according to age and sex, 73 per cent were male and 27 per cent female. The number of male cases of brucellosis exceeded the female in all age groups except the very young and those over 60.

More cases of undulant fever are reported during the summer months than during the cold season. This may be accounted for on the basis of increase (1) in discharges from infected animals following calving and farrowing, (2) in types of contact with infected animals, (3) in raw dairy products containing Brucella, and (4) in rate of multiplication of the organisms in dairy products owing to the higher temperature. In tracing undulant fever to the animal source, the agglutination test, blood culture and tests of animals and of milk specimens are the most important available methods. The control of the disease is dependent on measures of prevention of transmission through daily contact with infected animals or their environment. Prevention should be aimed especially at eradication of Bang's disease in cows, pasteurization of dairy products, vaccination, and limiting the chances for exposure in all forms of direct contact with animals that may be infected.

1. Jordan, C. F., and Borts, I. H.: Brucellosis in Iowa, Iowa Pub. Health Bull. **50**: 4 (July, Aug., Sept.) 1936.

ARTIFICIAL RADIOACTIVE MATERIAL

The possibility of applying artificial radioactive elements to biologic research and radiation therapy has aroused much interest. Some investigators have prophesied that artificial radioactive elements may eventually replace radium and radon for certain types of therapy.

M. and Mme. Joliot, son-in-law and daughter of the late famous Mme. Curie, were awarded the Nobel Prize (1934) for their discovery of artificial radioactivity. They bombarded boron with alpha rays, making a substance called radionitrogen, which gave off radiation resembling the radiation from radium. The life of the product, which is about fourteen minutes, is insignificant compared to the life of radium. Other investigators in many parts of the world have followed this line of research. For the bombarding medium some have

used the neutron, the electrically uncharged elementary particle possessing nearly the same mass as the hydrogen atom, and others have used the deuteron, the charged atom of heavy hydrogen. To date, more than forty elements have been made artificially radioactive, and the half-life of this radioactivity varies from a few seconds to about fourteen days.

In the radiation laboratory in the Department of Physics, University of California, a device called the cyclatron has been invented, which creates exceedingly high velocities of deuterons.[1] The high velocity of these deuterons is generated between the poles of a huge electromagnet. Essentially, its operation consists of deuterons being continuously accelerated round and round in a spiral. This gives them their high speed energy, which otherwise would be unobtainable. The deuterons reach a wall of one electrode and pass out of it through a slit; then they pass through a thin vacuum-tight metal window. Materials such as common salt are placed at this point. It is possible to bombard the sodium in the salt and make a product known as radiosodium. The half-life of radiosodium is fifteen and one-half hours. The chief advantages of these products would seem to lie in the homogeneity of their radiations, the suitability of their half-lives for therapeutic uses, and the nontoxicity of their decay products. Several other research laboratories have acquired cyclatrons, and more are obtaining them now.[2]

The life of the radioactive substance is short and therefore would probably not be as detrimental to the human being as radium when it is taken internally. More experimental work is required. At present it will be retarded because of the unavailability of machines to produce artificial radioactive materials. Other instruments have been developed for this purpose, but the cyclatron seems to present the greatest possibilities. Its bulk of several tons and its great expense necessarily restrict research activity except in localities where the cyclatron is available.

1. Lawrence, E. O., and Livingston, M. S.: The Production of High Speed Light Ions Without the Use of High Voltages, Physical Review **40**: 19-35, 1932.
2. Locher, G. L.: Biological Effects and Therapeutic Possibilities of Neutrons, Am. J. Roentgenol. **36**: 1 (July) 1936.

Current Comment

ORIGIN OF FECAL FAT

The products of digestion in the gastro-intestinal tract are not in the body until they have passed through the wall of the intestine. Two circumstances have combined to render difficult the precise determination of the so-called utilization of the major food materials and the evaluation of the factors influencing it; namely, the great difficulty in securing samples of blood and lymph at the immediate site of absorption from the intestine and the now well known fact that materials are excreted into the enteric canal as well as absorbed from it. Thus the fecal lipid may represent either unabsorbed fat, fat that has been excreted, or both. The presence of bile is an important factor in the digestion and absorption of fat; in its absence there is a definite increase in fecal fat. In order to determine the origin of the lipid in the feces of subjects with bile fistulas, Shapiro and his co-workers [1] have fed, together with the diet, fat containing a known proportion of deuterium. This isotope [2] of hydrogen apparently behaves as ordinary hydrogen in metabolism and yet can be quantitatively determined in compounds containing it; it serves as an identifying "mark" for substances of which it is a part. The proportion of deuterium in the fecal fat equated with that in the food fat should thus serve as a reliable index to the origin of the fecal fat. It was found that of the deuterium-containing fat given with the food only 30 and 35 per cent respectively appeared in the feces of the two subjects studied. It was concluded "from these analyses that the remaining 65 to 70 per cent of the diet fatty acid was absorbed and that the greater part of the fecal fat in our patients originated from the fat secreted into the intestinal tract." The subjects received 0.7 and 2.1 Gm. of the deuterium-containing fat in the diet; it appears that such small amounts of fat can be largely absorbed even in the absence of bile and that, if all the food fat followed the course of the deuterium-containing fat, fecal lipid in the absence of bile has, to a large extent, an endogenous origin.

CONTROL OF SYPHILIS

The Prosser White Oration, delivered by Dr. John H. Stokes before the St. John's Hospital and the London Dermatological Society, June 15, 1936, has been recently printed by the Public Health Service of the U. S. Treasury Department.[1] Much of this address considers the failure to control the spread of syphilis as effectively as present knowledge of the disease would imply. Stokes points out some shortcomings in the laboratory tests for syphilis. Thus, he believes that the darkfield examination has serious limitations as a practical diagnostic device. Similarly, the serologic tests for syphilis require a well organized mechanism, which partially inhibits their universal use. Furthermore, he points out as others have done that the clinical knowledge of the course and symptomatology of syphilis as well as the attempt to eliminate it is frequently underdeveloped in medical practitioners. The epidemiology of the disease also comes under consideration by Stokes. Modern treatment, while more effective than earlier methods, is more intricate and more prolonged and hence is frequently abandoned before optimal effects have been obtained. Stokes does not feel, however, that the clinic as such, as opposed to treatment by individual physicians, is the answer to the problem. He believes that better clinics rather than more clinics, and better trained physicians, should be more effective than requiring all treatment to be performed in clinics. Intensive effort with regard to the development of a public health policy for syphilis control and to widespread educational efforts offers the most promising method of controlling this still flourishing disease.

1. Shapiro, Arthur; Koster, Harry; Rittenberg, D., and Schoenheimer, Rudolf, Am. J. Physiol. **117**: 525 (Nov.) 1936.
2. Isotopes in Physiologic Research, Editorial, J. A. M. A. **105**: 1432 (Nov. 2) 1935.
1. Stokes, J. H.: The Control of Syphilis, Ven. Dis. Inform. **17**: 315 (Nov.) 1936.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

District Meeting.—The Ninth Councilor District Medical Society met at the Hotel Seville, Harrison, December 1. The speakers were Drs. Francis Walter Carruthers, Little Rock, on "Diagnosis and Treatment of Vascular Diseases of the Extremities"; Sidney J. Wolfermann, Fort Smith, "Early Diagnosis of Intestinal Obstruction"; Melvin E. McCaskill, Little Rock, "Congenital Defects of the Uterus"; Grady W. Reagan, Little Rock, "Principles of Treatment of Gonorrhea," and Charles T. Chamberlain, Fort Smith, "Common Colds."

CALIFORNIA

Dr. Porter Returns as Dean.—Dr. Langley Porter, who retired this year as dean of the University of California Medical School, San Francisco, has returned to the position at the request of President Robert Gordon Sproul. His appointment is effective immediately. He succeeds the late Dr. Williams McKim Marriott, who died shortly after taking over the duties of dean. Dr. Porter has been associated with the University of California since 1918.

Heart and Tuberculosis Study. — The California Heart Association has been organized with the following officers: Drs. John C. Ruddock, Los Angeles, president; John J. Sampson, San Francisco, vice president, and Howard F. West, Los Angeles, secretary-treasurer. The Los Angeles County Heart Association has been reorganized as a branch of the state group. It has been announced that a statewide program for the study and prevention of heart and vascular diseases will be undertaken cooperatively by the new California Heart Association and the California Tuberculosis Association. A cooperative program is also under way between the Los Angeles County heart and tuberculosis associations.

Third Annual Graduate Assembly. — The Alumni Association of the College of Medical Evangelists presented its third annual graduate assembly in Paulson Hall, Los Angeles, December 6. The following program was offered:

Dr. Harry E. Alderson, San Francisco, Rhinoscleroma—A California Problem.
Dr. John MacKenzie Brown, Los Angeles, Sinusitis in Children.
Dr. Curle Latimer Callander, San Francisco, A New Amputation Through the Thigh at the Knee.
Dr. James F. Churchill, San Diego, A Discussion of Cardiac Drugs and Their Uses.
Dr. Harold K. Faber, San Francisco, Prophylaxis of Communicable Diseases.
Dr. Alvin G. Foord, Pasadena, Laboratory Diagnosis for the General Practitioner.
Dr. Verne C. Hunt, Los Angeles, Surgical Treatment of Duodenal and Gastric Ulcers.
Dr. Alexander Ray Irvine, Los Angeles, Problem of the Cross-Eyed Child.
Dr. William J. Kerr, San Francisco, Obesity and Its Complications.
Dr. William S. Kiskadden, Los Angeles, Technic of Repair of Skin Defects.
Dr. Alfred E. Koehler, Santa Barbara, Functional Indigestion.
Dr. Verne R. Mason, Los Angeles, Hemoglobin.
Dr. James N. Nichols, Los Angeles, Surgery of the Aged.
Dr. Eberle Kost Shelton, Santa Barbara, The Thyroid and Pituitary Factors in Growth and Development.
Dr. Roy E. Thomas, Los Angeles, The Management and Specific Treatment of Lobar Pneumonia.
Dr. Howard F. West, Los Angeles, Deficiency Disease Conditioned by Gastro-Intestinal Pathology.
Dr. Montague S. Woolf, San Francisco, The Commoner Surgical Diseases of the Rectum and Anus.
Dr. Walter M. Dickie, director, state department of public health, Berkeley, Plague.

COLORADO

Personal. — Dr. Fred A. Forney, medical director of the Modern Woodmen Sanatorium, Woodmen, Colo., has been appointed medical director and superintendent, succeeding the late John E. Swanger.

FLORIDA

Society News.—Dr. Erasmus B. Hardee, Vero Beach, was elected president of the Florida East Coast Medical Association, November 14, at its annual meeting in Fort Pierce. Other officers are Drs. Frederick K. Herpel, West Palm Beach, and Frederick J. Waas, Jacksonville, vice presidents, and Elbert McLaury, Hollywood, secretary. The next annual session will be held in Hollywood. The Four County Medical Association (St. Lucie, Martin, Okeechobee and Indian River counties) acted as host and Dr. Melton D. Council, Fort Pierce, president, was toastmaster.

GEORGIA

Pediatric Meeting.—The fourth annual scientific session of the Georgia Pediatric Society was held in Atlanta, December 10, with the following speakers, among others:

Dr. Julius H. Hess, Chicago, Present Status of Serum Therapy.
Dr. John A. Toomey, Cleveland, Fundamental Unknowns in Infectious Diseases.
Dr. William A. Mulherin, Augusta, Observations on Southern Pediatrics.
Dr. Henry F. Helmholz, Rochester, Minn., Use of Mandelic Acid in the Treatment of Urinary Infections.

ILLINOIS

Questions Answered by Radio.—The state department of health has added a question box service to its weekly radio broadcast. The department will undertake to answer or discuss over the air questions of general interest concerning preventive medicine that may be submitted by listeners. Questions may be forwarded direct to the state department of public health at Springfield or to WGN, Chicago.

Chicago

Protection of Car for Society Members.—The Chicago Medical Society through its trustees will pay $50 for the arrest and conviction of any person forcibly entering or stealing the car of a member, or stealing a grip or instruments therefrom, or holding up a member while engaged in the practice of his profession during 1937. According to the society's bulletin, only one reward will be paid for convictions on combinations of the above offenses committed contemporaneously. A sticker will be given each member on payment of his 1937 dues, to be used for identification by the police department and other law-enforcing officers of Cook County.

IOWA

Releases for Newspapers.—The speakers' bureau of the Iowa State Medical Society inaugurated a program during November whereby weekly articles on medicine and health will be released to the newspapers in the state. The releases are prepared in the central office, approved by a censorship committee of five physicians and then mailed to the newspapers. A similar plan has been carried out in Wisconsin, Minnesota and Illinois.

State Journal Has New Editor.—Dr. Lee Forrest Hill, Des Moines, has been appointed editor of the *Journal of the Iowa State Medical Society*, effective January 1. He succeeds Dr. Ralph R. Simmons, who was recently promoted to be medical director of the Equitable Life Insurance Company of Iowa. Dr. Simmons has been identified with the state journal for about thirteen years, the first three of which he served as associate editor. He will continue in the latter capacity.

Dr. Haygood Deputy Health Commissioner.—Dr. Marvin F. Haygood, recently medical director of the Georgia emergency relief administration, Atlanta, has been appointed director of local health services for the Iowa State Department of Health. He will have charge of developing district and county health unit programs under the social security act, it is reported. Dr. Haygood will also become deputy health commissioner, succeeding Dr. Frederick J. Swift, who resigned to become superintendent of the Iowa Soldiers Home, Marshalltown. Dr. Haygood was once director of the county health work for the Georgia State Board of Health. He served as city health officer of Knoxville, Tenn., for six years and as superintendent of the Georgia Tuberculosis Sanatorium at Alto, five years.

Society News.—Dr. Karl A. Menninger, Topeka, discussed psychologic factors in medicine before the Pottawattamie County Medical Society in Council Bluffs, November 16.—— The Poweshiek County Medical Society devoted its meeting in Montezuma, October 13, to a discussion of medical economics; Dr. Joseph L. Ravitts, Montezuma, was the speaker. ——Dr. William D. Paul, Iowa City, discussed coronary heart disease before the Washington County Medical Society in Washington, October 26.——At a meeting of the Winneshiek County Medical Society in Decorah, October 13, Dr. Maurice C. Melrose, Independence, spoke on the treatment of varicose veins and ulcer.—— Dr. Edward H. Rynearson, Rochester, Minn., addressed the Woodbury County Medical Society in Sioux City, October 19, on recent advances in endocrinology. Dr. Louis M. Rosenthal, Chicago, addressed the society, November 19, on "Recent Advances in the Radiation Treatment of Cancer."

KENTUCKY

Society News.—Dr. John H. J. Upham, Columbus, Ohio, President-Elect of the American Medical Association, addressed the Jefferson County Medical Society, Louisville, December 21. ——Dr. Frank M. Stites Jr. addressed the Louisville Society of Physicians and Surgeons, December 17, on "Diseases of Later Life and Their Significance."

Restoration of Ephraim McDowell's Home.—At the annual session of the Kentucky State Medical Association in October, the committee on the Ephraim McDowell Memorial reported that the McDowell home in Danville has been purchased and is in the course of restoration as far as possible to the condition it presented at the time of Dr. McDowell's occupancy. Part of the purchase price was donated by the owners. For the remainder and for restoration purposes a WPA grant of $13,500 was obtained on the condition that the title to the property be vested in the state park commission. A fund of $10,000 has been raised from individual contributors, principally members of the Kentucky State Medical Association and the Southern Surgical Association, which also has a McDowell Memorial Committee. The committee also reported that the WPA architect has accumulated a collection of literature on Dr. McDowell, which will be placed in the memorial. It has been revealed that a building now being used as a pool room was undoubtedly Dr. McDowell's office and negotiations are under way to obtain it and restore it to its original state. The committee plans to have a bronze statue of the pioneer surgeon placed on the grounds if sufficient funds can be raised. Dr. Irvin Abell, Louisville, is chairman of the McDowell Committee and the members are Drs. Charles A. Vance, Lexington; Louis W. Frank and Arthur T. McCormack, Louisville; John Rice Cowan, Danville, and Carl C. Howard, Glasgow.

LOUISIANA

Society News.—The Orleans Parish Medical Society was addressed, November 23, by Drs. Emmerich von Haam and Charles R. Lafferty on "Etiology of Venereal Lesions"; Eugene B. Vickery, "Some Minor Disorders of the Female Urethra," and Michael E. DeBakey, "Surgical Treatment of Scleroderma."

The Chaille Memorial Oration.—The eleventh Stanford E. Chaille Memorial Oration of the Orleans Parish Medical Society was presented December 14. Instead of one speaker as formerly, the program this year was given by the following three speakers:

Dr. Donald C. Balfour, Rochester, Minn., The Etiology and Treatment of Peptic Ulcer.
Dr. Frederick A. Coller, Ann Arbor, The Administration of Fluid in the Surgical Patient.
Dr. Arthur W. Allen, Boston, Acute Abdominal Emergencies.

Dr. Bel Honored.—A banquet was given in honor of Dr. George S. Bel, professor of medicine, Louisiana State University Medical Center, New Orleans, December 3, in celebration of his recent appointment as director of Charity Hospital. Patients, former patients, city and state officials, and friends attended the dinner. Judge William W. Westerfield presided and speakers included Gov. Richard W. Leche, at whose birth Dr. Bel officiated, Judge Rufus E. Foster, and Drs. W. D. Phillips and Frederick L. Fenno. Dr. Bel is emeritus professor of the theory and practice of medicine and clinical medicine at Tulane University of Louisiana School of Medicine.

First New Orleans Graduate Assembly.—The First New Orleans Graduate Medical Assembly will be held March 8-11. Instruction, clinical demonstrations, didactic lectures, round table discussions, and symposiums will make up the program, which will be presented by the following speakers, among others:

Dr. Ralph M. Waters, professor of anesthesia, University of Wisconsin Medical School, Madison.
Dr. Albert C. Furstenberg, dean and professor of otolaryngology, University of Michigan Medical School, Ann Arbor.
Dr. Anthony Bassler, New York.
Dr. Frank Lynch, professor of obstetrics and gynecology, University of California Medical School, San Francisco.
Dr. Russell Cecil, professor of clinical medicine, Cornell University Medical College, New York.
Dr. Lewis J. Pollock, professor of nervous and mental diseases, Northwestern University Medical School, Chicago.
Dr. Henricus J. Stander, professor of obstetrics and gynecology, Cornell University Medical College, New York.
Dr. Clifford B. Walker, associate clinical professor of surgery (ophthalmology), University of Southern California School of Medicine, Los Angeles.
Dr. Robert B. Osgood, John B. and Buckminster Brown professor of orthopedic surgery, emeritus, Harvard University Medical School, Boston.
Dr. John A. Kolmer, professor of medicine, Temple University School of Medicine, Philadelphia.
Dr. Julius H. Hess, professor of pediatrics, University of Illinois College of Medicine, Chicago.
Dr. Rolla E. Dyer, U. S. Public Health Service, Washington, D. C.
Dr. Eugene P. Pendergrass, assistant professor of radiology, University of Pennsylvania School of Medicine, Philadelphia.
Dr. William W. Babcock, professor of surgery and clinical surgery, Temple University School of Medicine, Philadelphia.
Dr. Abernethy Benson Cannon, associate professor of dermatology, Columbia University College of Physicians and Surgeons, New York.
Dr. George Gray Ward, emeritus professor of obstetrics and gynecology, Cornell University Medical College, New York.
Dr. George Morris Piersol, professor of medicine, Medical Chirurgical College, Graduate School of Medicine, University of Pennsylvania, Philadelphia.
Dr. Hugh Trout, Jefferson Hospital, Roanoke, Va.
Dr. Meredith F. Campbell, clinical professor of urology, New York University College of Medicine, New York.

MARYLAND

Personal.—Drs. Arthur M. Shipley, professor of surgery, University of Maryland School of Medicine, and associate professor of surgery, Johns Hopkins University School of Medicine, and Louis P. Hamburger, associate in medicine, Johns Hopkins University School of Medicine, Baltimore, have been appointed consultants to the Baltimore City Health Department.——Elmer V. McCollum, Sc.D., Baltimore, has been appointed a member of the U. S. P. vitamin advisory board, succeeding the late Lafayette B. Mendel, D.Sc.——William E. Woodall, chief disinfector, Baltimore City Department of Health, recently resigned. He had been associated with the department since Nov. 1, 1902.

Society News.—Dr. Rolla E. Dyer, U. S. Public Health Service, discussed "Typhus and Rocky Mountain Spotted Fever" before the Baltimore City Medical Society at its annual meeting December 4. Dr. Morris Fishbein, editor of THE JOURNAL, addressed the society meeting jointly with the Osler Historical Society, December 18, on "Medical Bookplates." Dr. Francis R. Packard, Philadelphia, discussed case reports of Dr. Philip Syng Physick at the Pennsylvania Hospital.——The Allegany-Garrett County Medical Society was recently addressed by Drs. John P. Stump, New York, on "Prevention of Deformities in Arthritis" and George H. Preston, Baltimore, "The Problem of the Care of Mental Cases in Maryland."——At a recent meeting of the Baltimore County Medical Society, Dr. Milton B. Kress, Towson, among others, spoke on "Modern Concepts of Collapse Therapy."——The Frederick County Medical Society was addressed recently by Drs. Cyrus F. Horine, Baltimore, on "Empyema in Children" and George H. Preston, Baltimore, "Relationship of the Family Physician to the State Institutions Caring for the Mentally Ill."

MASSACHUSETTS

Society News.—Dr. Fletcher H. Colby, Boston, was chosen president of the New England Branch of the American Urological Association in Boston, November 12, and Dr. George C. Prather, Boston, secretary.——At a meeting of the Greater Boston Medical Society, December 1, Drs. Jacob Wallace, Gabriel J. Rubin, Harold J. Freedman, Morris Ingall and George Kahn discussed "Abdominal Pain in Infancy and Childhood."——Dr. Edwin B. Astwood, Baltimore, addressed the Harvard Medical Society, December 8, on "The Physiology of the Breast."——At a meeting of the Boston Pathological Society, December 1, Alfred Marshak, Ph.D., spoke on "Chromosome Structure, with Relation to Radiation," and Dr. Shields Warren, "The Effect of Radiation on the Skin."

Medical Extension Courses.—The Massachusetts Department of Education and the Massachusetts Society of Mental Hygiene began a series of lectures, November 12, on "Keeping Mentally Fit." With Dr. Henry B. Elkind, Boston, medical director of the state society for mental hygiene as the course leader, the lecturers include:

Joseph Jastrow, Ph.D., New York, Keeping Mentally Fit, November 12.
Dr. Douglas A. Thom, Boston, The Child: The Father of the Man, November 19.
Dr. Milton E. Kirkpatrick, Worcester, Adolescent Problems, December 3.
Dr. Abraham Myerson, Boston, Civilization and Its Discontents, December 10.
Dr. Jacob E. Finesinger, Boston, Practical Applications of Mental Hygiene, December 17.
Dr. Marianna Taylor, Boston, Moodiness and Fatigue, January 7.
Dr. Moses Ralph Kaufman, Cambridge, Psychoanalysis and Mental Health, January 14.

The lecturer to conclude the series, January 21, has not been announced.

MICHIGAN

Personal.—Dr. Susie Hurst Thompson, formerly of Gary, Ind., has been appointed in charge of district number 2 of the Children's Fund of Michigan, including the counties of Ogemaw, Alcona, Iosco and Oscoda, with headquarters in West Branch. She succeeds Dr. Gladys J. Kleinschmidt, Ann Arbor, who resigned November 1. This work is conducted in cooperation with the state department of health.

Model Constitution and By-Laws.—A special committee will be appointed to study the constitution and by-laws of each of the fifty-four county medical societies of Michigan with a view to developing a model set of regulations with principles conforming to the constitution and by-laws of the state medical society. At a recent meeting of the executive committee of the council of the state society, this step was unanimously approved.

Tribute to Physician.—Dr. David D. McNaughton, Argyle, was guest of honor at a banquet, November 30, given to celebrate his completion of fifty years in the practice of medicine in Sanilac County. The hosts were Drs. George Evans and Sanford Martin Tweedie, Sandusky, sons of the late Dr. George S. Tweedie, a close friend of Dr. McNaughton. He was president of the Sanilac County Medical Society from January 1925 to October 1927. He is 70 years old.

Society News.—Dr. Albert C. Furstenberg, dean and professor of otolaryngology, University of Michigan School of Medicine, Ann Arbor, discussed "Acute Suppurations of the Throat, Mouth and Cervical Region" before the Wayne County Medical Society, December 14, in Detroit. Dr. Roy R. Kracke, professor of pathology, Emory University School of Medicine, Georgia, addressed the society, December 21, on "The Leukopenic Diseases—Their Etiology, Diagnosis and Treatment."——At a meeting of the Jackson County Medical Society in Jackson, November 17, Dr. Edward G. Martin, Detroit, spoke on "Differential Diagnosis of Anorectal Diseases."

Dr. McLean Honored.—Dr. Angus McLean, Detroit, was formally presented with the Order of the Crown of Italy, with the degree of commander, at a banquet recently given in his honor. About 500 persons were in attendance, with Dr. James W. Inches as toastmaster. The presentation was made by the Italian consul, Enrico G. Belcredi, and speakers included Mr. Frank Cody, superintendent of the Detroit public schools and president of Wayne University, and Police Commissioner Pickert of Detroit. Dr. McLean was associated with his alma mater, the Detroit College of Medicine and Surgery, now the Wayne University College of Medicine, from 1905 to 1913 as professor of clinical surgery. He served as city physician from 1888 to 1892; quarantine inspector for the Port of Detroit, 1893, became a member of the state board of health in 1905, and, in 1911, a member of the Detroit Board of Health. He is a past president of the Wayne County Medical Society and of the Michigan State Medical Society.

MINNESOTA

University News.—The Center for Continuation Study at the University of Minnesota was dedicated, November 13-14. The building was financed in part by the PWA and contains living quarters and conference rooms, to be used for refresher courses of short duration.

Congress of Allied Professions. — Representatives of all professions allied in the delivery of medical care, including nurses, dentists, druggists, hospital executives and members of the bar, will be invited to an all day conference to be a feature of the eighty-fourth annual meeting of the Minnesota State Medical Association, St. Paul, May 3-5. The conference is scheduled for Monday; the speakers will include Dr. Morris Fishbein, editor of THE JOURNAL, Chicago; Father Alphonse M. Schwitalla, dean, St. Louis University School of Medicine, St. Louis, and Dr. Maxwell J. Lick, Erie, Pa., president of the Medical Society of the State of Pennsylvania.

MISSOURI

New State Health Commissioner.—Dr. Herman S. Gove, Linn, since 1934 director of the department of child hygiene, state department of health, has been appointed health commissioner of Missouri, succeeding Dr. Elmer T. McGaugh, resigned. Dr. Gove, prior to 1925, was for several years health officer of Osage County. In 1925 he was appointed a member of the state board of health, serving a term of six years, and in 1933 was appointed director of licensure in the office of the state health commissioner. Aged 57, Dr. Gove is a graduate of the Marion-Sims College of Medicine, class of 1901.

New Anatomical Society.—The organization of the Kansas City Anatomical Society was announced November 28. Dr. William Byron Black, president of the Kansas City Society of Ophthalmology and Otolaryngology, was elected president. Other officers are Drs. Albert N. B. Lemoine, Kansas City, and Lyman Robert Forgrave, St. Joseph, vice president; Willis E. Keith, secretary, and Oliver S. Gilliland, treasurer. Monthly meetings will be held by the new society, whose object is to offer postgraduate instruction. For the first three years the society's membership will be restricted to physicians interested in the eye, ear, nose and throat.

Memorial Meeting to Dr. Marriott.—A meeting in commemoration of the late Dr. W. McKim Marriott will be held in the auditorium of Washington University School of Medicine, St. Louis, January 3. Speakers will include Chancellor George R. Throop; Dr. Edwards A. Park, professor of medicine, Johns Hopkins University School of Medicine, Baltimore; Dr. Alexis F. Hartmann, professor of pediatrics at Washington, and Philip A. Shaffer, Ph.D., professor of biological chemistry and head of the department, Washington University School of Medicine. At the time of his death, November 11, Dr. Marriott was dean of the University of California Medical School, San Francisco, a position he assumed at the beginning of the school year. He had been dean of Washington University School of Medicine since 1923.

NEW JERSEY

Health at Trenton.—Telegraphic returns to the U. S. Department of Commerce from eighty-six cities with a total population of 37 million for the week ended December 19, indicated that the highest mortality rate (24.8) appeared for Trenton and the rate for the group of cities was 12.9. The rate for Trenton for the corresponding week of 1935 was 18.8 and that for the group of cities was 12.3. The annual rate for the eighty-six cities for the fifty-one weeks of 1936 was 12 as compared with 11.4 for the corresponding period of 1935. Caution should be used in the interpretation of these weekly figures, as they fluctuate widely. The fact that certain cities have a large Negro population or that they are hospital centers for large areas may tend to increase the death rate.

NEW MEXICO

Indian Service Meeting. — Dr. Marshall E. Burgess, Oraibi, Ariz., was elected president of the Indian Service Medical Society at its semiannual meeting in Albuquerque in November; Dr. James C. Hancock, Fort Apache, Ariz., was made secretary. Dr. William L. Lockman, Mescalero, read a paper on Malta fever and Dr. Hancock a paper on treatment of trachoma. The next meeting will be at Phoenix, Ariz., in the spring.

NEW YORK

Society News.—Dr. Edward K. Cravener, Schenectady, addressed the Medical Society of St. Lawrence County, November 19, on diseases of the hip joint in children.——Dr. Philip B. Barton, Amsterdam, discussed bronchoscopy in general medicine before the Medical Society of Fulton County, November 19.——Dr. Frederic E. Elliott, Brooklyn, addressed the Medical Society of the County of Nassau, Mineola, December 15, on "The Threat of Compulsory Health Insurance," and Courtney R. Hall, Ph.D., assistant professor of history at Adelphi College, Garden City, on "Medical History of Long Island."

Dr. Farrand to Retire from Cornell.—Dr. Livingston Farrand, president of Cornell University, Ithaca, since 1921, will retire June 30, it was announced recently. Dr. Farrand, now 69 years old, was graduated from the College of Physicians and Surgeons of Columbia University in 1891 and was instructor in psychology there from 1893 to 1901, adjunct professor of psychology from 1901 to 1903, and professor of anthropology from 1903 to 1914. In the latter year he became president of the University of Colorado and served there until March 1919, when he was made chairman of the central committee of the American Red Cross. He was with the Red Cross until appointed president of Cornell in October 1921. Among his other activities, Dr. Farrand was executive secretary of the National Association for the Study and Prevention of Tuberculosis from 1905 to 1914, editor of the *American Journal of Public Health*, 1912 to 1914, and director of tuberculosis work in France for the International Health Board of the Rockefeller Foundation, 1917-1918. Dr. Farrand has received many honors, including degrees from numerous universities and the decoration of the Legion of Honor of France. His successor at Cornell will be Edmund Ezra Day, Ph.D. (Harvard 1909), director for the social sciences of the Rockefeller Foundation since 1928 and of the General Education Board since 1933. He has contributed frequently to journals of psychology and anthropology.

New York City

Etching as a Hobby.—The fifth annual exhibition of the Haden Etching Club, composed of dentists and physicians who etch as a hobby, was held at the Leonard Clayton Gallery, December 1-12. This year work of the last five years was shown in addition to new plates. Exhibitors included Drs. Leigh H. Hunt, Jacob L. Maybaum, Benjamin F. Morrow, Henry Smith Williams, Jerome Selinger, Harold S. Vaughan and Joseph F. Saphir. Also included in the exhibit was a self portrait of Sir Francis Seymour Haden, famous English surgeon-etcher, lent by the artist's grandson. Dr. Leigh H. Hunt is honorary president of the club; B. W. Weinberger, D.D.S., president, and Charles Berger, D.D.S., secretary.

Personal.—John T. Hanks, D.D.S., former director of the division of dentistry in the New York City Department of Hospitals, died suddenly November 17 on a subway train, aged 66. Dr. Hanks was a member of the committee on community dental service of the New York Tuberculosis and Health Association, for several years chairman of the dental supplies division for the American Red Cross in New York, and a member of the economics committee of the American Dental Association. In 1934 Federal Emergency Relief Administrator Harry Hopkins appointed him consultant on dental care for the FERA. Recently he was appointed a member of the World's Fair committee. —— Joseph C. Hinsey, Ph.D., formerly professor of anatomy at Stanford University School of Medicine, San Francisco, has been made professor and head of the department of physiology at Cornell University Medical College. Dr. Hinsey succeeds Dr. Herbert S. Gasser, who became director of the Rockefeller Institute for Medical Research in July 1935.

Lectures on Heart Disease.—The New York Heart Association, the heart committee of the New York Tuberculosis and Health Association, is sponsoring lectures for practicing physicians on heart disease. The first four have been as follows: Drs. Robert H. Halsey, November 10, "Symptoms and Clinical Examination of the Cardiac Patient"; Clarence E. de la Chapelle, November 24, "X-Ray and Fluoroscopy of the Heart"; Robert L. Levy, December 8, "Clinical Electrocardiography"; Ernst P. Boas, December 22, "Hypertensive Heart Disease and Blood Pressure." The rest of the series will be:

Dr. Edwin P. Maynard Jr., Cardiovascular Syphilis, at the New York Academy of Medicine, January 12.
Dr. Eugene F. Du Bois, The Heart in Thyroid Disease, Cornell University Medical College, January 26.
Dr. Harold E. B. Pardee, Arteriosclerotic Heart Disease, New York Academy of Medicine, February 9 and 23.
Dr. Arthur C. DeGraff, Rheumatic Heart Disease, Bellevue Hospital, March 9 and 23.
Dr. Cary Eggleston, Treatment of Heart Disease, April 13 and 27.

There is no registration charge or admission fee.

Faculty Appointments at New York Medical College.—The following faculty appointments, among others, were recently announced by New York Medical College and Flower Hospital:

Drs. Robert S. Bickley and Henry Dawson Furniss, clinical professors of surgery.
Dr. Thomas Drysdale Buchanan, clinical professor of anesthesia.
Dr. Robin Hood, clinical professor of proctology.
Dr. Leon S. Loizeaux, clinical professor of gynecology and obstetrics.
Dr. Thomas Hodge McGavack, formerly of San Francisco, associate professor of medicine.
Drs. Edward J. McCabe and Ferdinand Montgomery Smith, associate clinical professors of surgery.
Drs. Harold E. Clark, Sexton C. Roane and Charles J. Goeller, assistant clinical professors of surgery.
Louis B. Dotti, Ph.D., assistant professor of physiology and biochemistry.
Dr. Edmund H. Hubner, assistant clinical professor of gynecology and obstetrics.
Dr. Guilford Allen Robinson, assistant clinical professor of radiology.
Dr. Paul M. Wood, assistant clinical professor of anesthesia.

Dr. Vincent T. Frankfurth, formerly assistant superintendent of the Michigan Farm Colony for Epileptics, Wahjamega, Mich., was made assistant medical superintendent of the Flower-Fifth Avenue Hospital. Miss Laura R. Logan, formerly director of nursing service at Cook County Hospital, Chicago, has been appointed principal of the school of nursing and director of nursing service at the hospital.

OHIO

Society News.—Dr. Paul B. Magnuson, Chicago, addressed the Montgomery County Medical Society, Dayton, December 4, on "Types and Cases of Arthritis."—Dr. James G. Carr, Chicago, addressed the Stark County Medical Society, Alliance, November 12, on "Treatment of Heart Disease." —— Dr. Anthony J. Lanza, New York, addressed the Mahoning County Medical Society, November 17, on "Trends in Medicine." ——Dr. William Allen Pusey, Chicago, addressed the Academy of Medicine of Cincinnati, December 8, on "Disease, Gadfly of the Mind, with Special Reference to the Stimulating Influence of Skin Disease." At a meeting December 15 the speakers were Dr. Sidney M. McCurdy, Columbus, medical supervisor of the state industrial commission, on "Our Medical Relations with Each Other"; Dr. Roy J. Secrest, Columbus, assistant supervisor, "Compensable Injuries from the Medical Standpoint," and Judge Thomas M. Gregory, chairman of the commission, "Problems Encountered in the Administration of Workmen's Compensation." —— Dr. Harve M. Clodfelter, Columbus, addressed the Muskingum County Medical Society at Zanesville, November 4, on "The Anemias and Their Treatment."

PENNSYLVANIA

State Tuberculosis Meeting.—The forty-fifth annual meeting of the Pennsylvania Tuberculosis Society will be held in Philadelphia at the Benjamin Franklin, January 19-20. There will be sessions on health education, the need for additional tuberculosis hospital beds and modern health needs and a medical session. Among the speakers will be Drs. Esmond R. Long, Philadelphia; Jay Arthur Myers, Minneapolis; Robert E. Plunkett, Albany, N. Y.; Kendall Emerson and Harry E. Kleinschmidt, New York.

Personal.—Dr. Edgar S. Buyers, Norristown, was recently elected president of the Montgomery County Medical Society after having served as secretary for twenty-one years. It is reported that he was absent only once and that when he was on official business for the society. Dr. Buyers is chairman of the board of trustees of the Medical Society of the State of Pennsylvania.——Dr. Paul C. McAndrew, Scranton, has been appointed medical director of the Lackawanna County Tuberculosis Sanatorium to succeed Dr. Frank R. Wheelock.

Philadelphia

Second Postgraduate Institute.—The Philadelphia County Medical Society announces its second annual Postgraduate Institute to be held at the Bellevue-Stratford, April 12-16. The subject this year will be "Diseases of the Chest and Upper Respiratory Tract."

Society News.—Dr. Charles H. deT. Shivers, Atlantic City, N. J., addressed the Philadelphia Urological Society, November 23, on "Newer Methods of Preoperative Study in Prostatic Hypertrophy."——Philip Bard, Ph.D., Baltimore, and Detlev W. Bronk, Ph.D., addressed the Philadelphia Neurological Society, November 27, on "The Significance of the Hypothalamic Representation of the Sympathetic Nervous System" and "The Control of Autonomic Activity and the Rôle of the Hypothalamus" respectively. At a meeting, December 18, the speakers were Drs. George M. Dorrance, on "Alcoholic Injection of the Gasserian Ganglion"; John Q. Griffith and Wilfred E. Fry, "Subarachnoid Hemorrhage with Special Reference to Papilledema," and Michael M. Scott, "Parietal and Cerebellar Lobe Atrophy Associated with Certain Cases of Multiple Sclerosis."

Pittsburgh

Society News.—Dr. Hugh H. Young, Baltimore, addressed the Allegheny County Medical Society, December 15, on "Medical and Surgical Problems in Diseases of the Prostate."—— Speakers at a meeting of the Pittsburgh Pediatric Society, December 11, were Drs. Hyman A. Slesinger, Windber, on "Pneumococcic Peritonitis"; Robert A. Knox, Washington, "Hyperinsulinism," and Ellsmer L. Piper, "A Study of the Initial Weight Loss in the New-Born."——At a meeting of the Pittsburgh Academy of Medicine, December 8, the speakers were Drs. Theodore Diller, on "Sexual Problems Which Confront the Medical Profession"; Alvan W. Sherrill, "Clinical Application of Fever Therapy," and Murray B. Ferderber, "Report of Cases Treated by Fever Therapy."

WASHINGTON

Dr. C. A. Smith Honored.—Dr. Clarence A. Smith, Seattle, editor of *Northwest Medicine* since its establishment in 1903, was the guest of honor at a dinner given by the King County Medical Society at the Rainier Club, November 23. Dr. Robert D. Forbes, president of the King County society, presided and gave a brief review of Dr. Smith's life. Dr. Frederick A. Kiehle, Portland, represented the Oregon State Medical Society with a tribute to Dr. Smith. Mr. Judson Jennings of the Seattle Library and Mr. Charles W. Smith of the library of the University of Washington gave talks of appreciation for Dr. Smith's part in the development of the Seattle Medical Library, which has been one of his major interests. Dr. Arthur C. Crookall, Seattle, president of the Washington State Medical Association, presented a watch on behalf of the assembled group and other friends. Dr. Smith, 75 years old, was graduated from Columbia University College of Physicians and Surgeons in 1887 and went to Seattle shortly afterward.

GENERAL

International Conference on Fever Therapy.—The first International Conference on Fever Therapy will be held at Columbia University College of Physicians and Surgeons, New York, March 29-31. The program is divided into four parts with committees in charge as follows: physiology, pathology and methods of production of fever, Drs. Frank W. Hartman, Detroit, chairman, and Charles A. Doan, Columbus, Ohio, secretary of the committee; miscellaneous diseases treated by fever therapy, Drs. Clarence A. Neymann, Chicago, chairman, and Frank H. Krusen, Rochester, Minn., secretary; syphilis, Drs. Walter M. Simpson, Dayton, Ohio, chairman, and Leland E. Hinsie, New York, secretary; gonorrhea, Drs. Stafford L. Warren, chairman, and Charles M. Carpenter, secretary, both of Rochester, N. Y. Those who wish to participate are requested to communicate with the chairman of the section in which they are interested and manuscripts must be submitted to the chairman before February 1. All who plan to attend are requested to register promptly with the general secretary, Dr. William Bierman, 471 Park Avenue, New York. The registration fee is $15. Baron Henri de Rothschild, Paris, is general chairman of the conference and Dr. Walter M. Simpson, Dayton, is chairman of the American committee.

Society News.—Dr. Edward Stanley Ryerson, Toronto, was elected president of the executive council of Nu Sigma Nu at the annual meeting in New Orleans, November 28. Dr. Stuart Graves, University, Ala., is secretary.——The forty-first annual meeting of the Seaboard Medical Association of Virginia and North Carolina was held at Tarboro, N. C., December 1-3. The guest speakers included Drs. Raymond A. Vonderlehr, U. S. Public Health Service, on "The Hidden Scourge"; Howard A. Patterson, New York, "Present Day Trend in Surgery of the Thyroid Gland"; James P. Hennessy, New York, "The Occipitoposterior Position," and Charles W. Mayo, Rochester, Minn., "Recent Advances in Cholecystic Disease." Dr. Philip St. L. Moncure, Norfolk, Va., was elected president and the following were elected vice presidents: Drs. Robert J. Walker Jr., Tarboro; Frederick C. Rinker, Norfolk, Va.; Thomas M. Watson, Greenville, N. C., and Albert A. Creecy, Newport News. Dr. Clarence Porter Jones, Newport News, was reelected secretary, and Virginia Beach was chosen as next year's meeting place.——The Clinical Orthopedic Society met in Dallas, Texas, October 30-31. Officers elected were Drs. James E. M. Thomson, Lincoln, Neb., president; James A. Dickson, Cleveland, vice president, and H. Earle Conwell, Birmingham, Ala., secretary. The 1937 meeting will be in Chicago.

Radio Forum on Growth of the Child.—Future lectures to be given in the radio forum on the growth and development of the child, under the auspices of the National Congress of Parents and Teachers, the American Academy of Pediatrics and the National Broadcasting Company, are as follows:

Dr. Alexander A. Weech, associate professor of pediatrics, Columbia University College of Physicians and Surgeons, New York, January 6, Energy and Growth.
Dr. Roy G. Hoskins, research associate in physiology, Harvard University Medical School, Boston, January 13, Our Glands.
Oscar Riddle, Ph.D., investigator, Station for Experimental Evolution, Carnegie Institution of Washington, Cold Spring Harbor, N. Y., January 20, The Action of Glands on Growth.
Otto Glasser, Ph.D., Cleveland, director, department of biophysics, Cleveland Clinic Foundation, January 27, Effects of Light, Sun and Other Rays on Growth.
Edwin C. MacDowell, Sc.D., Cold Spring Harbor, N. Y., investigator, Station for Experimental Evolution, Carnegie Institution of Washington, February 3, Heredity or Environment?
Dr. Arnold L. Gesell, New Haven, director, Clinic of Child Development, Yale University, February 10, How the Mind Grows in Infancy.
Walter R. Miles, Ph.D., professor of psychology, Institute of Human Relations, Yale University, February 17, How Children's Minds Grow.
Walter J. Damrosch, New York, February 24, Importance of Music for Growing Children.
John E. Anderson, Ph.D., director, Institute of Child Welfare, University of Minnesota, Minneapolis, March 3, Emotional Development in Children.
Dr. Bert I. Beverly, Chicago, assistant clinical professor of pediatrics, Rush Medical College, March 10, The Connection Between Mind and Body Growth.
Carleton Washburne, superintendent, public schools, Winnetka, Ill., March 17, Fitting the Course of Study to the Child's Mental Development.
Frank N. Freeman, Ph.D., professor of educational psychology, University of Chicago, March 24, Education and Mental Growth.
David B. Dill, Ph.D., associate professor of industrial physiology, Harvard Fatigue Laboratory, March 31, Athletics, Exercise and Fatigue in Growing Children.

The lectures are on the Blue network of the National Broadcasting Company every Wednesday from 4 to 4:30 p. m., Eastern Standard Time.

"Eye Specialist" Wilkinson Sentenced to Penitentiary.—The U. S. Post Office Department announces that Matthew O. Wilkinson, alias Dr. Billingsley, alias Dr. Clark, alias J. E. Clark, was sentenced to four years in the Virginia State Penitentiary following his plea of guilty, Dec. 2-3, in Bedford, Va., to a state charge of swindling Mr. S. B. Hawkins, Moneta, out of $625. Wilkinson, who was arrested in Milwaukee, August 31, and Harold N. Baxley, alias Jack Baxley, and Curtis Yeager, who were arrested in Pittsburgh, September 4, pleaded guilty to the same charge, the latter two being given five years each in the state penitentiary in Virginia. They had been arrested on charges of fraudulent use of the mails in connection with the collection of checks obtained from their victims in the "eyeswindling racket." According to the Post Office Department, December 11, these men will be tried later on the federal charges. When the authorities in California, where Wilkinson was wanted, were beginning to close in on him, he is said to have gone into other states to "practice." In May of last year the eyesight swindle was perpetrated in Arthur, Ill., by a man calling himself "Dr. Snyder of Tennessee." In 1933, in California, Wilkinson was identified through a photograph by a victim as the "Dr. J. C. Snyder" who had treated him. Elliott Wilkinson, said to be Matthew's brother, was also arrested in the recent round up, but no disposition of his case has yet been reported (THE JOURNAL, December 19, p. 2059).

Orthopedic Surgeons' Meeting.—The American Academy of Orthopaedic Surgeons will hold its fifth annual convention at the Hotel Cleveland, Cleveland, Ohio, January 10-14. The program will include clinical demonstrations and symposiums on shoulder disability, osteomyelitis, fractures of the ankle and low back pain. The speakers will include:

Dr. Merrill C. Mensor, San Francisco, Injuries to the Accessory Processes of the Vertebrae.
Dr. Charles W. Peabody, Detroit, Tendon Transference—Late Result Study.
Dr. Henry H. Kessler, Newark, N. J., The Cineplastic Amputation.
Dr. Charles Leslie Mitchell, Detroit, Phosphatase: Its Clinical Significance.
Dr. Wingate Todd, Cleveland, The Roentgen Ray in the Assessment of Growth and Health.
Dr. Frederick C. Kidner, Detroit, Torticollis.
Dr. Herman C. Schumm, Milwaukee, Schanz Osteotomy for Fracture of the Neck of the Femur.
Dr. W. Eugene Wolcott, Des Moines, Circulatory Studies and Nutrition of the Head of the Femur.
Dr. Samuel Kleinberg, New York, The Value of Early Weight Bearing in the Treatment of Fracture of the Neck of the Femur.
Dr. Paul C. Colonna, New York, Reconstruction Operation for Old, Ununited Fracture of the Femoral Neck.
Dr. Jose Valls, Buenos Aires, Argentina, New Technic for Nailing Fractures of the Neck of the Femur.
Dr. Charles B. Huggins, Chicago, Bone Marrow and Its Relation to Orthopedic Surgery.
Howard B. Lewis, Ph.D., Ann Arbor, Mich., Some Aspects of the Utilization of Sulfur Compounds in Health and Disease.
Dr. Halford Hallock, New York, Arthroplasty of the Hip Joint: An End Result Study of Seventy-Nine Unselected Cases.
Dr. Beveridge H. Moore, Chicago, Effect of the Periosteum on the Position of Fracture Fragments.
Dr. Albert B. Ferguson, New York, Roentgenologic Diagnosis of Tuberculosis of the Joints.
Dr. Dallas B. Phemister and Cly H. Hatcher, Chicago, Pathology of Hematogenous Osteomyelitis.
Dr. Edwin F. Cave, Boston, Tuberculosis of the Spine in Children.

There will be five radio broadcasts during the meeting: Drs. Melvin S. Henderson, Rochester, Minn., "The Accomplishments of Orthopedic Surgery"; Edwin W. Ryerson, Chicago, "Physically Handicapped Children and Adults"; Albert H. Freiberg, Cincinnati, "Infantile Paralysis"; Robert B. Osgood, Boston, "Recent Advances in Arthritis," and Willis C. Campbell, Memphis, "The Fracture Situation."

CANADA

Personal.—Dr. Thomas A. Patrick, Yorkton, Sask., received a desk set from his colleagues in the Northern Saskatchewan Medical Association at a meeting recently as a tribute to his long service as a physician, almost fifty years. Dr. Patrick graduated from the University of Western Ontario School of Medicine, London, in 1888 and the University of Manitoba Faculty of Medicine, Winnipeg, 1889.

University News.—McGill University, Montreal, recently announced a grant of $17,000 from the Rockefeller Foundation to cover a three year program of research in genetics and experimental cytology.——The following promotions at the University of Western Ontario, London, were reported in the *Canadian Medical Association Journal:*

Dr. George H. Stevenson to be professor of psychiatry.
Dr. William P. Tew, professor of obstetrics and gynecology.
Dr. Earle M. Watson, professor of pathologic chemistry.
Dr. Russell A. Waud, professor of pharmacology.
Dr. David W. Crombie, assistant professor of medicine.
Dr. Paul M. Andrus, assistant professor of radiology.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 21, 1936.

The Medical Uses of Radium

The report of the Medical Research Council on the medical uses of radium summarizes important recent work. At the Royal Cancer Hospital Dr. W. V. Mayneord has investigated the problem of radium dosage and the conversion of milligram hours into roentgens. The question has not been completely settled but there is general agreement among workers that 8 roentgens represents about the dose of radiation from 1 mg. of radium element screened with 0.55 mm. of platinum at a distance of 1 cm. for one hour.

THE CARCINOGENIC ACTION OF SCREENED RADIUM

Screened radium has been shown to be capable of producing the disease for the treatment of which it is most used. This research, by Dr. Joan Ross, is based on a case in which a radium needle, used in the treatment of cancer of the breast, became detached and penetrated the chest wall. Attempts to regain it failed and the patient died three years later from heart failure. At the necropsy the needle was found embedded in the interventricular septum of the heart, and there was in the liver a malignant hemangioma immediately under the site of the needle. The mode of spread of the growth through the liver tissue showed that its point of origin was in the part of the liver nearest the radium needle. This pointed to the conclusion that the presence of the needle so long adjacent to the position of the growth was the cause. Radium tubes 1 cm. long, each containing 0.1 mg. of radium screened with 0.55 mg. of platinum, were inserted into rabbits. These containers represent weak gamma-ray sources, the amount of hard beta-rays passing through being negligible. It was intended to open the peritoneum and anchor the tubes in the liver but this was found to be impracticable. After various trials one tube was placed in the chest wall on the right side close to the liver. Some shifting of the tubes occurred probably soon after insertion. Seven out of nine rabbits experimented on developed cancer in the immediate neighborhood of the tube. Six of the growths appeared at intervals between ninety-seven and 135 weeks, the seventh after 167 weeks. Five of the growths were sarcoma and two squamous-cell carcinoma. In all the cases of sarcoma except one (in which the animal was still alive) there were metastases in the lungs or elsewhere. One of the carcinomas had produced metastases in lymph glands and the lungs; the other did not show any. These experiments demonstrated the important fact that small amounts of highly screened radium acting for a sufficiently long period can produce malignant growths the character of which depends on the nature of the tissue in close proximity to the tube, though not in that immediately proximate.

CANCER OF THE BREAST

In cancer of the breast, radical operation is still the most usual treatment whenever practicable. At the Birmingham General Hospital, large and inoperable breast cancers have been treated with full doses of high voltage (200,000) x-rays. In some cases these tumors have been rendered operable from eight to ten weeks later. Microscopic examination of these irradiated breasts has almost invariably shown some islets of cancer cells surrounded by dense fibrous tissue. This raises the question of the advisability of removing such irradiated breasts and clearing out the axillae, even after radiation has caused disappearance of the tumor. At the Marie Curie Hospital, radical surgical removal is carried out whenever practicable. When radiotherapy is used, preference is given to the low intensity method of Coutard. During the past year smaller daily doses have been given over larger fields, with avoidance as far as possible of marked skin and connective tissue reactions.

CANCER OF THE MOUTH

The Aberdeen Royal Infirmary reports that, in carcinoma of the lower lip, radium element was used in twenty-one cases and radon in ten, with complete healing after a single treatment. Both the element and radon were fully screened and used interstitially. The impression has been gained that the early response to the radium treatment of secondary malignant nodes is improving.

Eight patients were treated for carcinoma of the tongue. In five the primary growth disappeared and the tongue healed after a single radium treatment. The radium was fully screened and the method was interstitial. In two cases the healed site was excised seven months after the radium treatment and no malignant cells were found on microscopic examination.

The Birmingham General Hospital reports that there is little difficulty in curing primary growths of the buccal cavity, provided the floor is not extensively involved. Effective treatment of secondaries in the neck is much more difficult. Radiation alone—whether radium or high voltage x-rays—rarely cures. The gland fields are treated by dissection, and as soon as the wound is sufficiently healed treatment by a radium collar or high voltage x-rays follows.

PARIS

(From Our Regular Correspondent)

Nov. 24, 1936.

Social Insurance Questions

Up to now, every worker who has no dependent children and who earns 21,000 francs (about $1,000, after devaluation of the franc) is obliged to take out social insurance. The employer pays a monthly premium equal to that paid by the worker. A worker who has two or more dependent children and who earns 25,000 francs must be insured. The government has recently proposed a law according to which these salary limits will be raised, so that a large number of workers not now insured will be obliged to join the social insurance organization. In a letter addressed by its president, Dr. Tissier, to the Federation of Medical Syndicates of France, dated August 6 and published in the September issue of the *Bulletin* of the Syndicate of Physicians of the Department of the Seine, the statement is made that, although the question of raising the limit of obligatory insurance is more of an economic than of a professional character, the extension of social insurance, especially in the region of Paris, to a considerably larger number of workers cannot fail to be of interest to the practitioners of this region. The application of the social insurance law has already affected the practice of medicine seriously and imposed a heavy burden, which the profession has accepted in a most loyal manner. Confronted with the proposed modification of the law, the profession feels itself entitled to claim an application of the law which will permit a physician at least to earn a living; hence the authorities are requested to consider the present plight of the profession in France before raising the limit of obligatory insurance. No one can ignore the loss of time, the vexatious examinations, the abusive investigations to which a practitioner is subjected in connection with the medical control demanded by certain caisses or bureaus which pay the claims for illness of the insured. This is especially true of patients treated by the practitioner at his office or at the home of the insured. These disagreeable encounters between the medical inspectors of the caisses and the practitioners, often taking place in the presence of the patients and tending to cause them to lose confidence in their medical atten-

dant, should in the future be avoided in the case not only of those already insured but also, if the proposed limit is raised, of those in the higher salaried brackets, who are more likely to consult a physician than those in the present lower brackets. The original law of 1930 had given the insured workers and their medical attendants a certain number of guaranties, such as free choice of physicians and the equitable adjustment of indemnities, which has induced the majority of the working class to accept the law. The law as modified in October 1935, which was not passed on by the legislature, added a number of restrictions, which have increased the power of the caisses or disbursing bureaus. The regional boards on which the organized medical profession is represented are seldom summoned to meet with the superior council of the social insurance organizations. The secretary of the federation, in his answer to this letter, stated that most of the abuses to which the local (Seine) organization had directed attention were only in the power of the main social insurance organization and its subsidiaries to correct. As to the higher limit of obligatory insurance, this will not go into effect, as proposed in the recent bill.

Discussion of Obligatory Retirement Bill

In the *Concours médical* of October 4 appears an analysis of the ideas of those members of the French chamber of deputies who are sponsors of the proposed Pomaret bill to oblige the members of all the liberal professions to surrender their licenses or diplomas when they have reached the age of 65 years and to retire without any thought of compensation by the government. The bill will come up for debate at the next session (November) of the chamber. In the article by Dr. Paul Boudin referred to, the sponsors of the bill are quoted as saying that "it is necessary to make places for those who wish to earn a living and establish a family. Social security demands the elimination of those who are enfeebled by age, i. e., whose intellectual and physical faculties are diminished as compared to those of younger individuals. Hence every profession should be organized from the corporative standpoint so as to permit all those who need repose to retire. No child should work before the age of 14, or 16, if possible. The public should be protected against quacks in every profession." Boudin comments on this by saying that but little has been done with regard to the last named in France. Such an exclusion of quacks would open up more places for the younger aspirants. The forced retirement law would not go into effect until Jan. 1, 1939, so as to permit the various professional groups to organize a system of pensions without, however, any aid from the government. Boudin heartily endorses the measures aiming to exclude quacks and discourage young men and women from overcrowding the liberal professions, as at present, by means of stricter entrance requirements and closer supervision during their courses in the professional schools. Every physician and dentist in France pays a relatively high tax, termed "patente," for the privilege of practicing. Boudin suggests that instead of this tax being paid to the state, it should be turned into a fund which shall serve as an endowment from which physicians or dentists shall be paid a pension should they choose to retire voluntarily at the age of 65. The various medical syndicates or unions are preparing to fight the Pomaret bill with all the resources at their command.

Increase in Cardiovascular Disease

In the June 27 issue of the *Presse médicale* two cardiologists, Lian and Cahana, state that the mortality of cardiovascular disorders is constantly increasing and at present exceeds that of pulmonary tuberculosis and cancer. This is shown in the tabulation of statistics for all of France, per hundred thousand inhabitants.

The principal reason for this increase in cardiovascular mortality is the longer average duration of life, which in the sixteenth century was twenty-one years, rising in 1900 to forty-seven years and in 1920 to fifty-four years. If one studies the statistics of cardiovascular mortality according to age, it is evident that it has increased only in those more than 45 years

Mortality in France

	1906	1911	1920	1930
Heart disease	120	115	106	139
Cerebral hemorrhage	83	86	80	80
Pulmonary tuberculosis	380	343	227	197
Cancer	114	112	128	130
Respiratory disorders	291	265	243	188

of age. The cardiovascular mortality has nearly doubled from 1900 to 1920 and tripled from 1920 to 1929 in persons more than 45 years of age. As the vascular diseases such as hypertension, angina pectoris and other coronary disorders, as well as atheromatosis in its various localizations, appear as a rule after the age of 40, it seems reasonable to conclude that the higher cardiovascular mortality is essentially due to the increased average duration of life. Deaths below the age of 40 represent only 3 per cent of the total number due to cardiovascular disease.

VIENNA

(From Our Regular Correspondent)

Oct. 22, 1936.

The First Austrian Roentgenologic Congress

The Austrian Society of Roentgenology held its first convention September 4-8 at Vienna. Professor Kienböck presided. The convention was attended by 300 leading roentgenologists from all parts of Europe; 119 prepared individual discussions were submitted and numerous discussions and demonstrations took place. The three principal topics under discussion and the men who introduced them by the reading of special papers were (1) "Roentgen Symptomatology as an Expression of Organic Function," Professor Leb of Graz, (2) "Clinical Practice and Methodology of Roentgen Cinematography," Professor Dessauer (a Jewish refugee from Germany, now residing in Istanbul), and (3) "Principles and Development of Roentgenotherapeutic Irradiation Procedures and Their Biologic Foundations," by Professor Schwarz of Vienna.

Professor Freund, himself the first to apply roentgen rays for therapeutic purposes, said in his introductory address that Vienna may be called the birthplace of roentgenotherapy. Freund recollected in this connection with what difficulty he established the new procedure as a part of the therapeutic armament. Any innovation that represents an advance of science has always at first to fight the battle for recognition. Freund said also that one might point with pride to the fact that Vienna has been the scene of a whole group of important developments in the field of roentgenology: roentgenotherapy, arteriography, pyelography, encephalography and other procedures.

The proceedings of the congress were arranged as follows: (*a*) Roentgenologic diagnostic methods for disturbances of the brain and spinal cord, the lungs and circulation, the digestive system and its subdivisions, the urinary passage, the female genitalia and the skeletal system. (*b*) The technic and physics of roentgenography: indirect and direct cinematography, kymography. (*c*) Roentgenotherapy: single session irradiation, saturation treatment, irradiation with extremely high voltage, distant irradiation, contact therapy. Combinations of therapeutic procedures: radium therapy in combination with roentgenotherapy; operative treatment in conjunction with radiotherapy. Moreover, some thirty papers on miscellaneous subjects were submitted.

Professor Leb of Graz, who spoke on the first principal topic, emphasized that the principal function of roentgenographic diagnostic procedure is the demonstration of anatomic changes within the human organism; with this, however, the possibilities of roentgen examination are by no means exhausted. Observations of the living organism disclose not only purely functional disturbances which often represent a preliminary stage of secondary anatomic disorders but other functional disturbances as well, by which whole pathologic syndromes may be established.

Of interest were papers by Professor Schüller of Vienna on the use of contrast solutions for demonstration of the cerebral cavities and by Löhr of Magdeburg on his own methodical investigation of the cerebral arteries. In the course of four years Löhr examined close to 900 cerebral and cranial lesions and arrived at the conclusion that disturbances of the vascular supply in the central nervous system, which are traumatic in origin, permit of remarkably good roentgen visualizations that are most helpful for prognosis. Professor Dyes of Würzburg, after considerable roentgenographic research on tumors of the brain, was able to make the following observations: In all tumor cases in which the seat is the lower posterior half of the posterior cranial fossa, enlargement of the ventricle is present. If, however, the seat is the upper and frontal half, enlargement of the fourth ventricle will be lacking but the three remaining ventricles will show enlargement. As long as the cerebrospinal fluid can enter the fourth ventricle the latter appears of normal size, and without further ado the seat of the tumor is in its lateral aspect to be determined. If the tumor is situated in the region of the sagittal suture, the upper part of the ventricle on the affected side is compressed. Tumors on the convexity present a similar picture. Tumors situated in the temporal region cause the ventricle of the affected side to appear concavely extended over the neoplasm. Excellent pictures of the respiratory mechanism were exhibited with the kymographion by Weber of Bern.

Schuster and Zdansky, both of Vienna, demonstrated how clearly alterations in the size of the heart following the performance of a single piece of work and different types of respiration may be portrayed by roentgenography.

A good part of the convention was taken up in discussion of the roentgenology of the gastro-intestinal tract. Although the lecture and reports on this topic were extremely interesting, by and large nothing fundamentally new was elucidated. Presser of Vienna discussed gastric tumors; Haas of Budapest, gastric motility; Ratkoczy, also of Budapest, circumstances that influence the gastric tonus. A sensation was produced by the explanations of Dillon of Moscow of the respiratory function of the digestive tract. By his experiments it was determined that man as well as many vertebrate animals and fish is capable of inhaling air into the stomach and intestine. The air is actually inhaled, not swallowed, and it may serve to assist respiratory function in general. Incontestable proof exists that it is possible for the organism to live for a certain time exclusively by means of the air inhaled into the digestive tract. Roentgen examination is therefore the best and most reliable test for the determination of whether a fetus will be born living or dead. In two cases cited by the author, new-born infants shown on necropsy to present complete atelectasis of both lungs had lived and cried, the one for a period of twenty-five minutes, the other for five hours.

Roentgen visualization of the appendix vermiformis and the causes of nonvisualization formed the subject matter of a large number of discussions.

Pape of Vienna gave a discussion of disturbances in the colonic power of locomotion and Werner of Bratislava a perhaps more important talk on the rapid testing of colonic function. By means of irrigoradioscopy supplemented by pneumography, the entire large intestine can be completely visualized within eight hours, thus making it possible for the examination to be concluded within the same day.

The importance of roentgenology in recent years has increased; especially noteworthy are the improved methods of demonstrating the intricate urinary passages. Urography of the process of elimination is a useful procedure for functional testing of the kidney and kidney pelvis, especially as it provides indication or contraindication of operative intervention. The first impetus to the research on renal function by means of roentgen rays began in Vienna, although as early as 1887 the physiology of the pelvis of the kidney was investigated by Israel in Berlin. Later on this type of research came to be carried on in various countries.

Simon of Vienna contributed observations on functional alterations in the urinary tract and in the large intestine during pregnancy. It was established that the gravid uterus not only acts by mechanical compression of the urinary tract and the large intestine but gives rise to physiologic disturbances of function in both regions and these may be both toxic and incretory in nature. The atonic and congested state of the organs usually disappears completely subsequent to the pregnancy.

Roentgen cinematography may be said to have aroused greater interest than any other subject before the congress. Janker of Bonn and Reynolds of London, in two lectures on cinematography, differentiated direct and indirect cinematography and concerned themselves with the last-named method. Its principle is the photographing of the fluoroscopic appearance; it is possible to take from twenty-five to fifty pictures a second by means of modern apparatus. Occasionally a rate of as many as 100 pictures a second may be attained. If the direct method is used the size of the single picture corresponds to any of the usual roentgenograms. Consequently the number of pictures in a second and the length of the film are greatly restricted, transportation is rendered much more difficult and the expense is great. By the indirect method one is certain to obtain quickly produced inexpensive and excellent pictures for the study of organic function. It was first used by Reynolds in London in 1920-1921 but at that time presented great difficulties, owing to the imperfection of the technic. As the picture may now be taken speedily and the period of exposure is brief, the procedure is now completely without danger to the patient. Both Janker and Reynolds exhibited truly marvelous pictures before the congress. Especially worthy of mention were the visualizations of cardiac movement, of the acts of swallowing and of speaking, of an embolism artificially produced in animal experimentation, of gastric activity, and of the movements of the larynx and tongue in speaking and singing—in the last named the sound of the voice was reproduced.

The direct method was demonstrated by Van de Maele of Brussels. It permits of a rate of some eight pictures a second and the production of excellent individual pictures. It permits furthermore of a close study of the details of motility in various organs.

Kymography too enlisted the interest of the delegates. It was discussed by Stumpf of Munich.

The discussions of roentgenotherapeutic questions formed the high point of the transactions. Prof. Gottwald Schwarz of Vienna outlined the historical development of this branch. He described the establishment of the generally accepted roentgenometric unit, the roentgen, which was proposed by Villard of Paris in 1908 but first adopted as an international unit twenty years later. Roentgenotherapy has been materially improved in recent years, by Coutard of Paris in particular.

Latterly the controverted question has been the relative merits of the single session method. There is also rivalry between

the fractionated and protracted fractionated methods of irradiation. Evaluations of distance irradiation and of contact therapy were also attempted by the congress.

Wintz of Erlangen advocated single irradiation. Young, rapidly growing cells (such as carcinoma cells) are quickly destroyed by large doses. Irradiation by a series of doses decreases the radioactivity of tumors. Application of even the smallest doses may cause a tumor to become radiorefractive. As a rule the healthy cells in the vicinity of a tumor show themselves more capable of resisting the roentgen rays. Saturation therapy was discussed by Holfelder of Frankfort. The effect of roentgen rays on a malignant growth is the stronger as the cancer cells are destroyed and the normal cells of the organism protected. This eventuates if the topographic trend of the tumor seat is exactly determined, the overlapping tissue layers delimited by means of a maximal compression and the tumor, so to speak, directly hit. Large doses are at first applied (full tolerance dose), followed by lesser doses for from four to eight weeks.

Coutard of Paris described the roentgen treatment of carcinoma by fractionated protracted daily irradiation and by irradiation in periodic series. This method has made possible the first permanent roentgenotherapeutic cures of carcinoma. The method is basic, dosimetric and quantitative. Its fundamental principle is the amount of the total dose and its physical distribution in space, irrespective of whether the daily dosage is strong or weak. Results are satisfactory only if the carcinoma is scarcely differentiated and infiltration has not yet set in and if the cells exhibit a considerable radiosensitivity that remains fairly constant during the treatment. The total dosage requisite for permanent cure did not as a rule differ greatly, no matter what the distribution. The dosages were from 6,000 to 8,000 roentgens for the larynx, from 7,000 to 8,500 for the pharynx and from 8,000 to 9,000 for the tonsils. The daily dose was around 500 roentgens in the shorter treatments and from 300 to 700 in the serial irradiation. The area of exposure varied from 50 to 125 sq. cm. It was interesting to note that if the total is greatly increased (to from 10,000 to 12,000 roentgens) the only result was deterioration and this was irrespective of the distribution of the application in point of time.

Schinz of Zurich, who spoke on the same topic, has customarily administered the simple fractionated irradiation when, because of the condition of the tumor, he could hope to achieve only a palliative effect. He resorted to the protracted fractionated procedure if the end result anticipated was not merely freedom from symptoms but permanent cure. When employing the first method he administered 1,500 roentgens within five days' time; in following the second method he administered from 4,000 to 15,000 roentgens, the amount depending on the seat of the tumor. Schinz, like Coutard, exhibited statistics on the successes and failures that he had experienced. Of interest are the data on mammary carcinoma. In the operable cases a protracted fractionated preliminary irradiation and a fractionated after-irradiation were administered, whereas in the inoperable cases three irradiations lasting fifty minutes each were administered every second day until a total dosage of 4,000 roentgens had been given, this requiring in all about fourteen days.

Pulmonary carcinoma was discussed by Popovic of Zagreb. In 30 per cent of seventy cases (sixty-eight men, two women, aged from 19 to 70) improvement, both subjective and objective, was obtained, but only two of the patients could be saved. Sgalitzer of Vienna discussed the methods of tumor irradiation in the central nervous system. His first choice was the fractionated method, by which, he said, severe manifestations were avoided. Roentgen treatment of cerebral disorders is best directed from several points of attack; extremely favorable results have been obtained from the use of this procedure in hydrocephalus. In brain tumor cases also, irradiation from four or five points of attack is beneficial. Whether the cranium is open or closed is an important consideration in irradiation. Radiotherapy is contraindicated if increased compression of the brain is present, excepting in cases of hypophyseal tumor. The optimal end result in brain tumors is anticipated from operation followed by roentgen irradiation. Postoperative irradiation acts favorably in glioma and sarcoma cases in which it has been impossible to effect a radical intervention.

Gunsett of Strasbourg spoke on irradiation with tension as high as 600 kilovolts. This method is chiefly suitable for deeply situated carcinoma. Hard rays should be used. The speaker has administered from 3,500 to 4,000 roentgens in from four to five weeks with a fair measure of success. E. Maier of Vienna spoke on distant treatment with radium. In this type of therapy the "r"-afflux applied per minute is minimal in proportion to the roentgen "r"-afflux. It represents but a fraction of the last-named type of energy and therefore distant irradiation with radium cannot be replaced by roentgen irradiation.

Schäfer of Greifswald discussed the use of contact therapy in gynecologic cases. This method has its advantages: the skin is completely protected by the introduction of certain tubes into the bodily cavities and it is possible to irradiate the parametrium with powerful doses; at the same time healthy tissue is completely protected by filters. Schäfer used irradiation in fifty-six cases of carcinoma of the female genitalia, 38 per cent of which were cases of inoperable carcinoma of the cervix uteri. The primary results were excellent; a check up showed twenty of the cervical cases to be negative, and only one case showed deterioration. The period of observation has been too short to permit conjecture as to end results. It may be said, however, that cases in which marked favorable effect is lacking undergo further deterioration.

Chaoul of Berlin discussed the method of close roentgen irradiation that bears his name. This method was used with satisfactory results in treating 307 patients who presented directly accessible cancerous growths. Patients were submitted to rays of the most promising strength (usually from 6,000 to 10,000 roentgens per field); the administration of the dosage was distributed over several weeks. Melchart of Vienna emphasized that the future method of combating cancer will be the combination of surgery with roentgen rays and at the same time with radium. Wessely and E. G. Mayer, both of Vienna, discussed the present attitude toward treatment of malignant tumors of the upper respiratory and digestive tracts. In very severe cases irradiation should be introduced first and surgical intervention later; frequently the procedure must be reversed in order that the tumor may receive direct irradiation; this would be done in carcinoma of the accessory nasal cavities. Carcinoma of the inner larynx and of the pharynx with metastases in the glands, conditions in which extensive operative intervention was formerly indicated, are now, following the Coutard method, only irradiated.

Radon was discussed as a separate topic by several research scholars, among whom were Happel of Hamburg, Uhlmann of Istanbul and Wasserburger of Vienna. Among disease conditions that react well to this type of therapy are exophthalmic goiter, lymphangiomas, keloids, wounds that tend to heal imperfectly and small epitheliomas.

The report of Ziedses des Plantes of Utrecht created something of a sensation. It dealt with serioscopy, a technic that makes possible by means of multiple exposures the visualization of the body in a whole series of parallel planes, each of which may be considered separately. Among other independent discussions were those by Windholz of Vienna on roentgenotherapy of tumors and hyperplasias of the reticulo-

endothelial system (leukemia, xanthomatosis, blastomatoid alterations). All these conditions were favorably influenced by roentgen and radium irradiation.

The paper of Freund of Vienna on the problem of occupational injuries from irradiation has yet to be mentioned. Prolonged exposure to roentgen rays produces a condition of general debility, best manifested in the morphologic hematograms. Leukocytes decrease permanently to around 5,000; the whole picture of chronic roentgen intoxication is quite like benzene intoxication as determined by the American Benzene Commission. Therapeutic measures consist of exposure to natural or artificial sun rays of all wavelengths, fresh air, gymnastics, and a regimen of unboiled milk, liver and bone marrow. In desperate cases blood transfusion together with the extirpation of the spleen is recommended. The best therapeutic measure, however, is removal of the patient from the injurious occupational surroundings.

AUSTRALIA

(From Our Regular Correspondent)

Nov. 15, 1936.

A Commission to Study Hospital Lotteries

The government of South Australia appointed a royal commission to inquire whether it is desirable to institute lotteries in South Australia for the purpose of raising funds to assist in the finance of hospitals and other charitable institutions. The commission took evidence in the different states of the commonwealth and had special statistical information about lotteries of Great Britain, Ireland, France, the United States and Canada. The commission expressed itself in its report as being not unduly influenced by the religious or ethical aspect. It says it would not have felt justified in coming to its conclusion or objecting to the lottery system on the ground of ethical objection, if on other grounds it had been found desirable. There is a real difference in principle between a government on the one hand taxing private betting or other private activities of the people and on the other hand introducing a lottery for the purpose of raising money for one of its essential social services. In the former case the government takes no part in the promotion of the activities on which the tax is levied. In the case of a lottery, parliament either directly or through a department established by it promotes the lottery for the purpose of profit and takes an active part in inducing people to subscribe to it. No Australian government urges people by advertisement to bet on horse races in order that more revenue may be obtained from betting or to go to the pictures so that the amusement tax revenue may be increased, but when there are lotteries the public is definitely encouraged to do so.

The commission was much impressed in the course of its investigations by what appeared to be the political repercussions of lotteries either conducted by governments or under a government license. The commission gained the definite impression that lotteries conducted on the lines of those of New South Wales, Queensland and Tasmania tend to become the masters rather than the servants of the government that "controls" them. The commission considered that the state of affairs tends to demoralize governments. After full and careful investigation the commission satisfied itself that the lottery does not and cannot solve the hospital finance problem. Even in Ireland the immense Irish sweep has not relieved the government or the local authorities of their hospital obligations, and in Western Australia and in Queensland lotteries have not helped the government to any material extent. The existence of lotteries in four of the six Australian states, and the seeming benefits derived from them, give an impression that a lottery is desirable. After thorough investigation, however, the commission is satisfied that these benefits are more superficial than real.

It may appear difficult to understand why it is that, with all the revenue that lotteries bring in, the government or local authorities do not secure corresponding relief. There are several contributing factors to this position: 1. The people of Australia are becoming more and more hospital minded, which means an increasing demand for accommodation. 2. The existence of a lottery tends to create in the people a demand as of right for a much higher standard of hospital buildings and equipment, and for more hospitals. 3. The practice has been generally to use lottery moneys for capital expenditure and therefore the cost of maintenance necessarily increases. 4. The existence of a lottery tends to decrease the voluntary contributions for hospital and charitable purposes, and this factor is greatly accentuated when there is a rate or tax for hospitals as well. 5. Where charities are associated with lotteries, the charitable institutions set up higher standards. 6. It may be that one of the reasons why lottery moneys are spent in the manner in which they are is that such expenditure provides an excellent advertisement for the lottery. For these reasons the commission found that the establishment of a lottery will not materially relieve the government or the local governing authorities of their burdens for hospitals or charities. In fact, because of the higher standard that is built up through the expenditure of lottery moneys as capital the ultimate burden is likely to be increased by the existence of a lottery.

Everywhere says the report there is a tendency to increase the prizes and especially the first prize; and everywhere the lottery is an exploitation of the gullibility of the public and the widespread gambling instinct. In fact, so deep seated has this legalized form of gambling become that it is doubtful whether any government would dare to introduce legislation to abolish these lotteries. The commission concluded that a lottery as a form of hospital finance provides an unstable method that is demoralizing to the government, distinctly injurious to traders and detrimental in the end to the poorer sections of the community, who contribute the bulk of the receipts. If the people who buy lottery tickets can easily afford the money, they can afford to pay their share of the direct taxation necessary to support hospitals. If they cannot afford the money, the state should not take their money. From the establishment of the "golden casket" in Queensland nearly twenty years ago the total receipts amounted to £12,000,000, the prize money amounted to £7,000,000 and the sum paid to hospitals and charities after payment of expenses was £3,000,000. These figures confirm the commission in its belief that the lottery does not and cannot solve the hospital finance problem and consequently it was recommended that the practice should not be permitted in South Australia.

Marriages

ALEXANDER C. LEONARDO, Washington, D. C., to Miss Alleen L. Bingham of Greensboro, N. C., Sept. 15, 1936.

LAYMAN R. HARRISON, Long Island, N. Y., to Miss Claire C. Colligan of Morristown, N. J., Oct. 3, 1936.

JOHN WATTS FARTHING, Rochester, Minn., to Miss Esther Constance Tasa of Northfield, Sept. 26, 1936.

GLENN GREY PERRY to Miss Agnes Adelaide Williamson, both of High Point, N. C., in October 1936.

WILLIAM DEWEY HALL, Raleigh, N. C., to Miss Sue Ruth Hutto of Gaston, S. C., Oct. 17, 1936.

CRAWFORD DARY DUNHAM, New York, to Miss Margaret Todd of Butler, N. J., Oct. 17, 1936.

JOHN LOUDEN HILLHOUSE to Miss Virginia Jacobs, both of Birmingham, Ala., Oct. 10, 1936.

EDGAR LLOYD ROTHFUSS, Williamsport, Pa., to Miss Grace Clark of Carlisle, Sept. 8, 1936.

AL F. HOLLEY, Brewton, Ala., to Miss Vivian Thaxton at Porter in September 1936.

AUGUST M. HASEWINKLE, Markle, Ind., to Miss Rowena Dickman recently.

Deaths

Warren Stone Bickham, formerly instructor in operative surgery at the Columbia University College of Physicians and Surgeons, New York, the New York Post-Graduate Medical School and Hospital and the New York Polyclinic Medical School and Hospital, aged 75, died Dec. 1, 1936, at his home in New York, of pneumonia and cardiovascular disease. Dr. Bickham was born in Shreveport, La., Aug. 23, 1861. He attended the University of the South, Yale University and the University of Louisiana and in 1887 received the M.D. degree from Tulane University of Louisiana Medical Department, New Orleans, and from the College of Physicians and Surgeons, Medical Department of Columbia College. For several years Dr. Bickham practiced in New Orleans, where he was visiting surgeon to the Charity Hospital, junior surgeon to the Touro Infirmary and demonstrator of operative surgery at Tulane. He later came to New York and, among other positions, was surgeon in charge of general surgery at the Manhattan State Hospital. He was the author of a well known textbook on "Operative Surgery," published in 1903, and seven volumes on "Operative Surgery," the last volume published in 1933. In 1906 he contributed sections on Amputations and Ligations in "Keen's System of Surgery." He had just completed a treatise on "Amputations and Artificial Limbs." Dr. Bickham was a fellow of the New York Academy of Medicine and of the American College of Surgeons. In 1925 he was awarded the honorary degree of doctor of laws by Tulane University.

Charles Metcalfe Byrnes ⊕ Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1906; member of the American Neurological Association; past president of the Philadelphia Neurological Society; demonstrator in anatomy at his alma mater from 1902 to 1903; instructor in clinical neurology in 1909 and associate since 1918; adjunct professor of anatomy at the University of Virginia Department of Medicine, Charlottesville, 1906-1909; lecturer in neuropathology at the University of North Carolina in 1935; neurologist to the Church Home and Infirmary; visiting neurologist to the Baltimore Eye, Ear and Throat Hospital; consulting neurologist to the Peninsula General Hospital, Salisbury, Md.; contributed to Forchheimer's Therapeusis of Internal Diseases in 1913 and Tice's Practice of Medicine in 1920; aged 55; died, Nov. 29, 1936.

James Allison Hodges ⊕ Richmond, Va.; University of Virginia Department of Medicine, Charlottesville, 1883; member of the House of Delegates of the American Medical Association in 1923; emeritus professor of clinical, nervous and mental diseases at the Medical College of Virginia, and for many years president of the University College of Medicine; in North Carolina served as a member of the state board of health, associate editor of the *North Carolina Medical Journal;* fellow of the American College of Physicians; past president of the Richmond Academy of Medicine and member of the board of trustees; past president of the Medical Society of Virginia; in 1903 established the Hygeia Hospital and Sanatorium, which operated until 1920; aged 78; died, Dec. 15, 1936, at Greensboro, N. C.

Thomas Long Catterson, Spokane, Wash.; Detroit College of Medicine, 1887; member of the Washington State Medical Association; past president of the Spokane County Medical Society; fellow of the American College of Surgeons; at one time county physician and president of the city board of health; for many years on the staff of the Sacred Heart Hospital; aged 79; died, Oct. 20, 1936, of arteriosclerosis and senile dementia.

William Louis Chapman ⊕ Providence, R. I.; Boston University School of Medicine, 1897; member of the staff of St. Joseph's Hospital; on the editorial staff of the *Rhode Island Medical Journal;* was awarded the Alvarenga Prize of the College of Physicians of Philadelphia and the Fiske prizes of the Rhode Island Medical Society for various essays; music critic for local newspapers; aged 62; died, Nov. 15, 1936.

William H. Bohart, Vero Beach, Fla.; Rush Medical College, Chicago, 1891; formerly a practitioner in Chicago; at one time assistant clinical professor of surgery, Loyola University School of Medicine, Chicago; formerly on the staffs of St. Bernard's and Englewood hospitals, Chicago; for many years chief surgeon to the Chicago and Eastern Illinois Railroad Company; aged 67; died, Nov. 14, 1936.

Alphonso Nicholas Codd, Spokane, Wash.; Jefferson Medical College of Philadelphia, 1919; member of the Washington State Medical Association, the American Academy of Ophthalmology and Oto-Laryngology and the Pacific Coast Oto-Ophthalmological Society; aged 42; on the staffs of St. Luke's Hospital and the Sacred Heart Hospital, where he died, Oct. 31, 1936, of pneumonia.

William B. Wolf ⊕ Baltimore; College of Physicians and Surgeons, Baltimore, 1896; member of the American Urological Association; fellow of the American College of Surgeons; formerly associate professor of genito-urinary diseases, University of Maryland School of Medicine; on the staff of the Maryland General Hospital; aged 67; died suddenly, Nov. 1, 1936.

James Joseph Boucher, Hartford, Conn.; College of Physicians and Surgeons, Baltimore, 1904; member of the Connecticut State Medical Society; fellow of the American College of Surgeons; on the staff of the Mount Sinai Hospital and St. Francis Hospital; aged 61; died, Nov. 14, 1936, of an accidental gunshot wound, while hunting in Colombia.

William Porter Ellis ⊕ Painesville, Ohio; Cleveland Medical College, 1896; Cleveland College of Physicians and Surgeons, Medical Department Ohio Wesleyan University, 1903; past president of the Lake County Medical Society; at one time member of the state legislature and coroner of Geauga County; aged 66; died, Nov. 8, 1936, of heart disease.

Ray Arthur Edson, Buffalo; University of Buffalo School of Medicine, 1907; member of the Medical Society of the State of New York, and the American Academy of Ophthalmology and Oto-Laryngology; assistant professor of ophthalmology at his alma mater; on the staff of the Buffalo General Hospital; aged 54; was found dead, Nov. 5, 1936.

Jacob Clinton Atwell ⊕ Butler, Pa.; Medico-Chirurgical College of Philadelphia, 1898; fellow of the American College of Physicians; past president of the Butler County Medical Society; served during the World War; on the staff of the Butler County Memorial Hospital; aged 62; died, Nov. 2, 1936, of pneumonia.

Mary J. MacDuffee, Devon, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1898; formerly on the staffs of the Children's and Polyclinic hospitals, Philadelphia; aged 86; died, Oct. 16, 1936, in the Presbyterian Hospital, Philadelphia, of arteriosclerosis and gangrene of the left leg.

Ralph Raymond Harris ⊕ Columbus, Ohio; Starling Medical College, Columbus, 1903; served during the World War; chief medical officer of the Veterans Administration in Cincinnati; on the staffs of the Grant and White Cross hospitals; aged 57; died, Nov. 12, 1936, of chronic myocarditis.

Frank Webster Garber ⊕ Muskegon, Mich.; Rush Medical College, Chicago, 1888; past president of the Muskegon County Medical Society; fellow of the American College of Surgeons; on the staffs of the Hackley Hospital and the Mercy Hospital; aged 77; died, Nov. 9, 1936, of coronary thrombosis.

Joshua Shipley Devries ⊕ Fremont, Neb.; Omaha Medical College, 1888; formerly county and city physician and coroner; past president and secretary of the Dodge County Medical Society; on the staff of the Lutheran Good Samaritan Hospital; aged 72; was found dead, Nov. 15, 1936.

Edwin A. Long, Johnson City, Tenn.; University of Louisville (Ky.) Medical Department, 1891; member of the Tennessee State Medical Association; at one time city health officer; on the staff of the Appalachian Hospital; aged 74; died suddenly, Oct. 27, 1936, at Palmer, Va., of myocarditis.

William Albert Dearman ⊕ Whitfield, Miss.; Tulane University of Louisiana Medical Department, New Orleans, 1906; fellow of the American College of Physicians; assistant superintendent of the Mississippi State Hospital; aged 58; died, Nov. 4, 1936, of a self-inflicted bullet wound.

Thomas Vincent Buckley, Girardville, Pa.; Medico-Chirurgical College of Philadelphia, 1910; member of the Medical Society of the State of Pennsylvania; deputy coroner; aged 52; died, Nov. 6, 1936, in the Sacred Heart Hospital, Allentown, of cerebral hemorrhage.

Charles Eduard Max Fischer, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; formerly associate professor of medical biology, histology and embryology at his alma mater; aged 55; died, Nov. 16, 1936.

H. Manning Brabham, Ehrhardt, S. C.; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; member of the South Carolina Medical Association; aged 70; died, Nov. 19, 1936, in the Tri-County Hospital, Orangeburg, of injuries received in a fall.

Alton Bartlett Simonson, Elsie, Mich.; Detroit College of Medicine and Surgery, 1926; member of the Michigan State Medical Society; on the staff of the Clinton Memorial Hospital, St. Johns; aged 35; was instantly killed, Oct. 22, 1936, in an automobile accident.

Joseph P. Smyth ✠ Chicago; Rush Medical College, Chicago, 1888; clinical professor of medicine, Loyola University School of Medicine; on the staffs of St. Bernard's Hospital and the West Side Hospital; aged 74; died, Dec. 15, 1936, of coronary thrombosis.

Fairfax Irwin ✠ Senior Surgeon, U. S. Public Health Service, Washington, D. C.; University of Pennsylvania Department of Medicine, Philadelphia, 1877; served during the World War as adviser on sanitation for the U. S. Navy; aged 82; died, Oct. 28, 1936.

William Frederick McBride ✠ Dayton, Ind.; Rush Medical College, Chicago, 1895; past president of the Tippecanoe County Medical Society; aged 65; died, Oct. 4, 1936, in a hospital at Lafayette, of a benign tumor of the prostate and myocarditis.

Mott Hunton Arnold, San Diego, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; member of the California Medical Association; aged 53; died, Dec. 9, 1936, of coronary sclerosis.

Francis Marion Davis ✠ Greenville, N. C.; Harvard University Medical School, Boston, 1931; on the staff of the Pitt Community Hospital; aged 32; was instantly killed, Nov. 15, 1936, in an automobile accident near Morehead City.

James Edmund Downs, San Diego, Calif; College of Physicians and Surgeons, Keokuk, Iowa, 1878; Rush Medical College, Chicago, 1889; aged 82; died, Oct. 16, 1936, of hypostatic pneumonia and chronic myocarditis.

Walter Louis Finn, Iuka, Ill.; Missouri Medical College, St. Louis, 1899; member of the Illinois State Medical Society; state senator; served during the World War; aged 61; died suddenly, Nov. 7, 1936, of angina pectoris.

Allen Collins Butterfield ✠ Grand Rapids, Mich.; Grand Rapids Medical College, 1906; aged 59; on the staff of St. Mary's Hospital, where he died, Nov. 13, 1936, of embolism, following an operation for appendicitis.

Edward Alfred Brace, Ellington, Conn.; University of Vermont College of Medicine, Burlington, 1911; served during the World War; aged 57; died, Oct. 22, 1936, in the Veterans Administration Facility, New York.

John D. Dunham, Pattonsburg, Mo.; College of Physicians and Surgeons, Keokuk, Iowa, 1877; member of the Missouri State Medical Association; formerly member of the state legislature; aged 81; died, Oct. 6, 1936.

Starr Ford, Cincinnati; Medical College of Ohio, Cincinnati, 1897; formerly instructor in medicine at the University of Cincinnati College of Medicine; served during the World War; aged 71; died, Nov. 16, 1936.

Theodore Tillman Shackelford, Haskell, Okla.; University of Louisville (Ky.) Medical Department, 1910; past president of the board of education; served during the World War; aged 50; died, Oct. 18, 1936.

Charles Roy Vickery, South Bend, Ind.; Hahnemann Medical College and Hospital, Chicago, 1901; member of the Indiana State Medical Association; aged 65; died, Oct. 10, 1936, of coronary thrombosis.

William S. Stewart, Finleyville, Pa.; Medico-Chirurgical College of Philadelphia, 1887; served during the World War; past president of the board of education of Braddock; aged 72; died, Oct. 19, 1936.

John A. Tuthill, Le Roy, Ill.; State University of Iowa College of Medicine, Iowa City, 1881; formerly mayor and member of the school board; aged 81; died, Oct. 7, 1936, of angina pectoris.

Edward Richardson Gardner ✠ Montrose, Pa.; Jefferson Medical College of Philadelphia, 1882; secretary of the Susquehanna County Medical Society; aged 83; died suddenly Nov. 3, 1936.

Norman Halkier Goodenow, Los Angeles; Rush Medical College, Chicago, 1892; member of the California Medical Association; aged 66; died, Oct. 14, 1936, of subacute bacterial endocarditis.

Mearle C. Fox, Westlake, Ore.; Willamette University Medical Department, Salem, 1909; member of the Pacific Coast Oto-Ophthalmological Society; aged 54; died, Oct. 31, 1936, in Los Angeles, of heart disease.

Willis Wade Rutland, Lagrange, Ga.; Southern Medical College, Atlanta, 1889; aged 73; died, Oct. 24, 1936, in the Dunson Hospital, of pyelonephritis and hypertrophic prostatitis.

John Irvin Gossett, Rule, Texas (registered by Texas State Board of Medical Examiners, Act of 1907); aged 61; was found dead in bed, Oct. 24, 1936, of coronary thrombosis.

George W. Torrey, Chicago; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1895; also a dentist; aged 65; died, Dec. 12, 1936, of coronary thrombosis.

John Logan Avey, Los Angeles; University of Louisville (Ky.) Medical Department, 1891; served during the World War; formerly state senator; aged 71; died, Oct. 17, 1936.

Joseph Henry Witt, Waco, Texas; Tulane University of Louisiana Medical Department, New Orleans, 1885; aged 80; died, Oct. 27, 1936, in a local hospital, of senility.

Henry Adolph Siebenborn, Brooklyn; Cornell University Medical College, New York, 1899; aged 76; died, Oct. 26, 1936, of carcinoma of the right lung and arteriosclerosis.

Henry S. Hadsel, Oxford, Ohio; College of Physicians and Surgeons, Keokuk, Iowa, 1882; member of the Iowa State Medical Society; aged 84; died, Oct. 6, 1936.

Neils Alfred Peterson, Soldiers Grove, Wis.; Milwaukee Medical College, 1901; member of the State Medical Society of Wisconsin; aged 59; died, Oct. 30, 1936.

Albertus G. Greenawalt, Runnells, Iowa; Kentucky School of Medicine, Louisville, 1893; aged 68; died, Oct. 13, 1936, in Des Moines, of carcinoma of the pancreas.

Elisha L. Lee, Bridgeport, Ala.; University of Nashville (Tenn.) Medical Department, 1872; for many years bank president; aged 96; died, Oct. 16, 1936.

Thomas E. V. Fariss, Fairfield, Iowa (licensed by Iowa State Board of Medical Examiners in 1886); aged 90; died, Oct. 15, 1936, of myocarditis.

Harold Talbot Cartwright, East Rockaway, N. Y.; Long Island College Hospital, Brooklyn, 1917; aged 47; died, Oct. 25, 1936, of coronary occlusion.

John Eddowes Beebe, Chicago; Gross Medical College, Denver, 1895; aged 84; died, Nov. 14, 1936, of coronary thrombosis and arteriosclerosis.

John Francis Keenan, Brentwood, Md.; Howard University College of Medicine, Washington, D. C., 1885; aged 79; died suddenly, Oct. 12, 1936.

Robert Wilfred Moss Clark, Niagara Falls, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1934; aged 32; died, Oct. 25, 1936.

James Percival Leahy, New Bedford, Mass. (licensed in Massachusetts in 1902); aged 61; died, Oct. 31, 1936, of coronary thrombosis.

Samuel Breese Smith, Chicago; Dartmouth Medical School, Hanover, N. H., 1893; aged 73; died, Oct. 8, 1936, of cerebral hemorrhage.

Lewis Gaddy, Los Angeles; University of Tennessee Medical Department, Nashville, 1905; aged 66; died, Oct. 22, 1936, of arteriosclerosis.

John Scoular Goodfellow, Morrisburg, Ont., Canada; Trinity Medical College, Toronto, 1894; aged 65; died in October 1936.

Melbourne F. Keith, Moncton, N. B., Canada; University of the City of New York Medical Department, 1882; died in October 1936.

Willis A. Mansfield, Washington, Ill.; Chicago Medical College, 1884; aged 78; died suddenly, Oct. 30, 1936, of heart disease.

Frank Lewis Anderson, McIntire, Iowa; Louisville (Ky.) Medical College, 1893; aged 67; died, Oct. 20, 1936, of erysipelas.

Henry L. Bartlett, Templeton, Calif.; Northwestern University Medical School, Chicago, 1901; aged 66; died, Oct. 5, 1936.

Alonzo L. Share, Oklahoma City; Detroit College of Medicine, 1892; aged 72; died, Oct. 6, 1936, of cerebral hemorrhage.

E. W. Robberson, Gainesville, Texas (licensed in Texas under the Act of 1907); aged 85; died in October 1936.

Jacob Jacobson, St. Louis; Missouri Medical College, St. Louis, 1892; aged 67; died, Oct. 31, 1936, of heart disease.

Milton B. Deck, Bennet, Neb.; University of Maryland School of Medicine, Baltimore, 1879; died, Oct. 4, 1936.

Correspondence

ACCELERATED SERUM SICKNESS

To the Editor:—In their article on "The Therapy of (Horse) Serum Reactions" in THE JOURNAL, Nov. 21, 1936, Fantus and Feinberg state that the symptoms of "accelerated serum sickness" are "similar to those described under serum sickness" and that "the manifestations may differ in no way from those previously described in serum sickness, but usually they are much more severe and alarming."

Some authorities on this subject still confuse two entirely different phenomena; namely, allergic shock and serum sickness. The only symptom in common is urticaria and even this symptom is occasionally lacking. (Waldbott, G. L.: The Prevention of Anaphylactic Shock with a Study of Nine Fatal Cases, THE JOURNAL, Feb. 6, 1932, p. 446.) Allergic shock is always the result of a previously existing sensitization, regardless of whether or not it is inherited or acquired, and is characterized only by allergic symptoms. This reaction is due to an overdose of antigen above the individual's tolerance and —as it does in the anaphylactic animal experiment—it establishes a greater protection against the antigen in the patient. It is true that occasionally death has occurred so rapidly, particularly following intravenous or accidentally intravenous injections, that no symptoms could be observed. While such a situation accounts for greater difficulties in diagnosis, my experience with reactions following injections of pollen extract has given me sufficient clinical data to identify such an asymptomatic reaction definitely with allergic shock. The other type of reaction ("serum sickness" or "serum disease") is the expression of certain immunologic changes in the system of the nonallergic or allergic person which, as the authors admit, renders the individual either sensitive or more sensitive to this antigen. Its clinical course parallels closely that of an acute infection with hyperpyrexia and joint and glandular swelling and is at great variance with any manifestations observed in allergic diseases. The two types of reaction behave in the same characteristic manner regardless of what antigen is injected. (Waldbott: "Allergic" Shock from Substances Other Than Pollens and Serums, *Ann. Int. Med.* **7**:1308 [April] 1934.)

Various other statements in this article are open to criticism: In view of the fundamental experiments of Bret Ratner, many find it difficult to adhere to the old theory that allergic shock can occur only in naturally sensitive individuals and that the same symptom complex should be called "anaphylactic" shock if the patient's sensitivity is assumed to be acquired. This more or less theoretical question becomes of profound practical importance when the authors advocate, as they do, a different treatment for both types of shock and state that to the "naturally sensitive" patient no horse serum should be given "under any circumstances or in any way." Even if a distinction between acquired and natural sensitivity on the basis of different types of antibodies and heredity were possible, there is not the slightest evidence either experimentally or clinically that human sensitivity responds differently to treatment according to its origin. I believe this is true regardless of whether or not man can be "completely" desensitized in contrast with the anaphylactic animal, an observation which is partially responsible for the distinction of "anaphylactic" and "allergic" shock.

The authors do not state that "accelerated serum sickness" is actually an intensified form of allergic shock which is due either to an accidental puncture of, and injection into, a small vein or to extreme sensitivity to serum which is administered subcutaneously. Accordingly, they do not discuss one of the most useful measures for preventing these dangerous reactions, namely, the guarding against an accidental puncture of venules, by selecting the proper site of injection, by repeated withdrawals of the plunger before and during the injection for evidence of blood, by watching for bleeding after the injection, and by other precautions recently outlined elsewhere by M. S. Ascher and myself. (The Rôle of Accidental Puncture of Veins in the Production of Allergic Shock, *Ann. Int. Med.* **9**:1232 [March] 1936).

The value of rapid hyposensitization cannot be summarily dismissed, as it is done by the authors, merely because its original technic as advocated by Besredka and Freeman is not devoid of danger. There is increasing evidence that this method can be carried out as a safe procedure. Since our preliminary report on this subject (Rapid Hyposensitization, *J. Allergy* **6**:93 [Nov.] 1934), Ascher and I have studied more than 300 patients treated with this method. We found that rapid hyposensitization is not only safe but in many instances the method of choice when quick action is needed. The key for its success lies in observing the following points: the starting with a sufficiently low dose, the careful gaging of subsequent doses, and the adjustment of the time interval between injections as determined by the degree of the local swelling from each individual injection.

GEORGE L. WALDBOTT, M.D., Detroit.

THE INDIFFERENCE OF OUR MEDICAL SCHOOLS TO CAREERS IN PUBLIC HEALTH

To the Editor:—A recent inquiry into progress of New Mexico medical students in the field of public health reveals an astonishing lack of interest on the part of the deans of our medical schools in public health as a career for their future graduates.

In the last Educational Number of THE JOURNAL (Aug. 29, 1936, p. 664) was given a list of the medical schools showing the students registered by the state of their birth. It happens that in New Mexico only physicians who have lived for two years in this state are eligible for positions in the field of public health. In order that a record of eligible physicians in the younger age groups might be available in our office, I wrote to the dean of each school where New Mexico students are registered the following letter:

> On page 664 of the Educational Number of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION I find that .... New Mexico students are registered in your school. I am very anxious to keep a record of the medical students from this state who may possibly become interested in public health service in order that the most promising of them may have an opportunity of postgraduate study in public health at the expense of the state if they are unable to afford such postgraduate study themselves. To this end I have prepared a card index and am enclosing herewith the cards relative to the students in your school and would be very grateful if you would be so good as to have them completed and returned to this office.

Of the nineteen so addressed, five did not answer at all. Of the remaining fourteen, only three replied to the inquiry regarding the student's interest in a career in public health, unless it was to say that of course they could not reply to this inquiry. Most deans apparently made the assumption that we should ask the student himself about his interest. While there was a general spirit of willingness to cooperate in this investigation on the part of the deans, only three medical schools showed a sense of responsibility in seeking to secure for their graduates an opportunity to pursue a career in public health. They were the University of Chicago, the University of Colorado and the College of Medical Evangelists in Los Angeles.

It is not clear whether this indifference to the student's future career is limited to the field of public health or whether perhaps deans of medical schools differ from the deans of other schools in feeling that a student's future career is entirely his own business and that the university has no responsibility in regard thereto.

J. ROSSLYN EARP, DR.P.H., Santa Fe, N. M.
Director, New Mexico Bureau of Public Health.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

GLYCOSURIA IN PNEUMONIA AND OTHER INFECTIONS

To the Editor:—July 14, 1936, I sent to the hospital a youth of 20, very sick with left lower lobar pneumonia, marked cyanosis, a temperature of 103 F., pulse 130, respiration 48, pink sputum, vomiting frequently for the past two days, and taking almost no nourishment. At the hospital, oxygen was at once administered. The white blood count was 23,500 and blood sugar 0.166 Gm. per hundred cubic centimeters. The pneumonia proved to be type II. Immediately I had 10 units of insulin given by hypodermic injection, repeated three times daily for the next two days and then reduced to 4 units for two days, with none thereafter. The blood sugar on admission at noon after two days of vomiting was 0.166 Gm.; next morning (the 15th) it was 0.136 Gm., on the 16th it was 0.090 Gm. before breakfast and on the 20th after breakfast it was 0.111 Gm., the day of discharge from the hospital. The patient had no history of diabetes. Urine specimens were negative for sugar. He never cared for sweets. In THE JOURNAL, Jan. 18, 1936, page 259, is a brief abstract from Moscow telling of Drs. Sinelnikov, Perchik and Doroklova testing twenty-three cases of pneumonia, all showing high blood sugar and recovery occurring in all but one on the administration of insulin. I have not been able to locate other studies of blood sugar in pneumonia or severe acute colds. As a result of my observation I should invite further studies. A number of problems present themselves: 1. Is high blood sugar frequently present in pneumonia cases? If so, would not this provide a good growth medium for the offending bacteria? 2. If the blood sugar is usually high in pneumonia cases should not insulin be a natural additional weapon in combating pneumonia? 3. If high, when did blood sugar rise in any case of pneumonia? Was it during the prepneumonic upper respiratory infection? If so, could early giving of insulin possibly be a new means of preventing some pneumonias? 4. In the cases of high blood sugar, what is the cause of the sudden hypo-insulinemia (if it is such), toxemia, anoxemia or otherwise? Numerous other questions could be suggested. Owing to the remarkably speedy recovery in the case reported following the mentioned observation, I felt that widespread good could come to other physicians handling similar cases and possibly stimulate the study of blood sugars in pneumonias in various centers of the country. HENRY RAILE, M.D., Salt Lake City.

ANSWER.—Transient glycosuria has often been noted in infectious diseases. It has been found in diphtheria, scarlet fever, typhoid, influenza, infections with suppuration, Asiatic cholera, malaria, carbuncle or gangrene, and pneumonia.

A lowered dextrose tolerance was reported by Hamman and Hirschman in lobar pneumonia and acute tonsillitis (*Arch. Int. Med.* **20**:761 [Nov.] 1917). Abnormal blood sugar curves in many acute infections were found by Olmsted and Gay, by Labbé and Boulin and by Andresen and Schmidt. Patients with oral sepsis or general sepsis frequently have a lowered carbohydrate tolerance. A deficient metabolism of carbohydrates has been described by Pemberton in arthritis.

Animal experiments by Rosenthal, by Tisdall, Drake and Brown, by Sweeney and Lackey and by Williams and Dick also indicate a decreased tolerance for dextrose in experimental infections.

It is now well known that infections in patients with diabetes mellitus cause a marked reduction of dextrose tolerance, and large doses of insulin are necessary to control an acidosis in such patients. An acute infection may be the precipitating cause of coma in a diabetic patient. Diabetes not infrequently develops after some acute infectious disease (typhoid, scarlet fever, influenza, diphtheria, tonsillitis, syphilis, rheumatic fever, mumps, focal infection, pneumonia). Diabetes may accompany or follow an acute pancreatitis, and some writers claim a relationship to gallbladder disease.

The toxemia of infectious diseases most likely reduces the production of insulin, as insulin injections restore the carbohydrate tolerance. The toxic products of many bacteria have a harmful effect on the islets of Langerhans and may either cause diabetes mellitus to develop or aggravate the disease if it is already present. In any infectious disease in which a definite disturbance of carbohydrate metabolism develops, insulin will be of value in sparing the islets and thus aid in the recovery or regeneration of these structures.

Williams and Dick (*Arch. Int. Med.* **50**:801 [Dec.] 1932) studied the dextrose tolerance in 108 patients with acute infectious diseases. There were eight cases of pneumonia. The amount of dextrose in the twenty-four hour urine averaged 1.66 Gm. Three of these patients were reexamined after the crisis, with an average of 0.83 Gm. In two patients the reduced tolerance persisted long after recovery from the pneumonia and it was necessary to restrict carbohydrates for several weeks. In two of five influenza patients there was a decided loss of tolerance. These two authors found that in patients with acute infections the most marked decrease in tolerance usually occurred in those who were severely ill or who had complications, or in those in whom two or more contagious diseases occurred in quick succession. The fasting blood sugar was found to be high in some cases of pneumonia. Warren and Root (*Am. J. Path.* **1**:415 [July] 1925) have described necrosis of the islet cells in pneumonia.

From the data it is evident that a temporary glycosuria occurs in many acute infectious and contagious diseases. This is accompanied by an increased fasting blood sugar and reduced carbohydrate tolerance. There is most likely some damage to the islets of Langerhans with a reduced insulin production. The decreased tolerance may last for weeks or months. Insulin injections improve the tolerance for dextrose.

A high blood sugar is often found in pneumonia, and in such patients the use of insulin would be of definite value. The tendency to feed large amounts of carbohydrate may be a factor in exhausting the islet cells.

Insulin is an additional weapon in combating pneumonia in diabetic patients only so far as it improves the metabolism and general condition of the patient and thus increases resistance to the pneumococcus. It has been demonstrated that types I and II pneumococci are rarely found in healthy throats but are often found in the throats of persons in contact with type I and II pneumonia patients. Individuals who are exposed to pneumococci and who do not possess sufficient immunity will contract the disease.

The blood sugar rise in pneumonia is due to the toxemia and therefore develops after invasion of the lung and perhaps the blood stream by pneumococci. It cannot at present be stated that a prepneumonic infection of the upper respiratory tract leads to pneumonia because it sometimes causes a rise in the blood sugar. The prevention of pneumonia is based on a satisfactory immunization against the toxic agent of the pneumococcus and isolation of the patients with this disease.

In the cases presenting a high blood sugar the cause of the hypo-insulinemia is most likely damage to the islets of Langerhans produced by the toxic polysaccharides found in the capsule of the pneumococcus.

ASTHMA

To the Editor:—Please describe the procedure in testing the sensitivity of patients suffering from asthma from causes in the home. Is any new symptomatic treatment being given now? I will appreciate any information with regard to the newer views and treatment of patients with asthma. Please omit name if published. M.D., Georgia.

ANSWER.—Several procedures may be followed. The safest method is to do scratch tests first. This consists of scarifying the skin, going through only the most superficial layers and being very careful not to draw blood. Twentieth normal sodium hydroxide is applied to the scratch and a small quantity of the dried allergen is rubbed into the sodium hydroxide. These materials may be purchased through several of the drug houses. The most common inhalant offenders are cottonseed, kapok, wool, silk, house dust, feathers, orris root, pyrethrum, mohair, cow hair, dog hair, cat hair, horse dander, rabbit hair and flaxseed. If these are negative, intracutaneous tests with sterile liquid extracts may be tried, the prescribed concentrations being used. A further procedure that may be used is to take samples of various materials in the home, soak them in twentieth normal sodium hydroxide for a few hours, and use the supernatant fluid for scratch tests.

If any materials give reactions, they should be completely removed from the environment. If this is impossible, such objects as mattresses and pillows may be covered with rubberized cloth, with double stitching and tape used over the seams.

Of course, complete pollen and food tests should also be done. Molds have been shown to be factors in the etiology of some cases of asthma and should also be used in testing such a case.

The foods that react positively are eliminated from the diet. The pollens and molds that react are used for treatment.

For symptomatic treatment epinephrine hypodermically and ephedrine orally are still most important. Epinephrine may also be given by inhalation in 1:100 solution in a special nebulizer (De Vilbiss No. 44). Sedatives, as bromides, the barbiturates or chloral hydrate, are frequently of marked benefit. In intractable asthma, whisky, especially at night, tends to relieve the spasm.

Vaccines (autogenous or stock) may be used intracutaneously in gradually increasing doses.

Nonspecific protein therapy by means of injection of peptone, typhoid vaccine or milk protein may be used.

If inhalants such as house dust are used in treatment, they are best given intracutaneously.

Recently several reports on desensitization with histamine have appeared in the literature (Dszinich, A.: *Klin. Wchnschr.* **14**:1593, 1935). Iodized oil instilled into the trachea has yielded good results in cases in which bronchiectasis is associated (Anderson, W.: *J. Allergy* **4**:44 [Nov.] 1932). Inhalation of helium gas has been reported (Barach, A. L.: *Ann. Int. Med.* **9**:739, 1935); also carbon dioxide inhalation (Farago, P.: *Ztschr. f. d. ges. exper. Med.* **91**:114, 1933), acid therapy (Beckman, H.: *J. Allergy* **1**:496 [Sept.] 1930), desiccated suprarenal gland (Barbour, D.: *Arch. Pediat.*, March 1, 1936), dextrose intravenously (Matzger, E.: *J. Allergy* **3**:599, 1932) and ether anesthesia in intractable asthma (Troisier, J., and Boquien, Y.: *Bull. et mém. Soc. méd. d. hôp. de Paris* **47**:310 [March 2] 1931).

LYMPHEDEMA OF LEGS

To the Editor:—A woman, aged 45, has had swelling of the right leg from the knee downward, for the past two years. In the morning the swelling is down, but toward evening the right leg is twice the size of the left leg. The swelling does not pit on pressure and the leg does not produce pain. The surface temperature seems the same as on the left leg. The only complaint the patient has is that she resents the massiveness and appearance of the limb when reminded by her friends of the difference in size. She refuses to wear an elastic stocking. When she came to me on her first visit I ruled out hernia and appendicitis. No operations had been performed. There was no liver enlargement, abdominal disturbance, dysuria, nocturia or urinary frequency. The specific gravity of the urine was 1.030. There was no albumin or sugar. Blood pressure was 150 systolic, 80 diastolic. Treatment consisted of Diuretic no. 1, Niemeyer's blue mass squill and digitalis, 1 grain (0.065 Gm.), one tablet every four hours for four days, Apiol and Digitalis tablets made by Upjohn, potassium citrate, 5 grains (0.3 Gm.), one of each after meals with one-half glass hot water. One week later the blood pressure was 140/82, the leg was less swollen, and the medication seemed to improve the condition. One month later she returned for treatment again. In the meantime she had the foot roentgenographed and it showed no bony pathologic changes or misplacements. A foot specialist taped the foot and prescribed an anklet to be worn. Every time I repeat the medication the leg becomes less swollen; as soon as medication ceases, the swelling returns. If the kidney is responsible for this impaired circulation, why doesn't the edema appear bilateral? Could a stricture of the saphenous opening be a cause for this condition? The patient has had one child; could there be an association of childbirth with this condition? The impairment of circulation seems to be localized, and the peculiar thing is that there is no pitting on pressure. Could this be one of those rare cases in which there is an impairment in the circulation of the lymphatics; but wouldn't this cause pitting? If there is a cirrhosis of the liver present, shouldn't there be a bilateral phenomenon rather than a localized condition? I am at a loss to inform the patient as to the cause of the swelling and I don't want to resort to the continued use of pills to allay the condition but would rather have you advise me as to how I should handle the case and advise the patient accordingly. I did not examine this woman internally to ascertain the presence of a fibroid, which might be responsible to vessel pressure internally and may cause impeded circulation.

P. R. EVANS, M.D., Tower City, Pa.

ANSWER.—The fact that only one leg is involved and that there is no evidence of constitutional disease, particularly of the heart or kidneys, strongly suggests that the swelling is due to local disease. Such a condition could arise as a result of chronic venous insufficiency caused by old thrombophlebitis or obstruction of the iliac vein from pressure, such as that exerted by a pelvic tumor. In thrombophlebitis the onset of swelling in the leg is usually fairly abrupt. In venous insufficiency that is caused by external venous pressure, it is more gradual. In either event the superficial veins of the lower part of the affected leg should be abnormally prominent and should empty more slowly than those of the other leg on elevation of the legs above the level of the heart. A more likely possibility is that this is a case of chronic lymphedema. In lymphedema it may be difficult to demonstrate actual pitting of the skin. The skin becomes coarse and thick, and the superficial fascia becomes markedly thickened and fibrotic. A roentgenogram taken for detail of the soft tissue will reveal the presence of a marked mottling in the subcutaneous region, caused by lymph pockets. Lymphedema may be attributable to recurrent episodes of lymphangitis of the skin which simulate local erysipelas. It may be caused by sclerosis of the iliac and inguinal lymph nodes resulting from lymphangitis, or it may be caused by invasion of the pelvic lymph vessels and lymph nodes by malignant tumors. Some cases of lymphedema are associated with trichophytosis of the feet, but in this type, as well as in the type that is caused by filariasis, there are usually recurrent episodes of lymphangitis and lymphadenitis. In another group are the congenital and hereditary types of lymphedema. A still further group, designated as lymphedema praecox, appears without any recognizable etiologic factor. (Allen, E. V., and Ghormley, R. K.: Lymphedema of the Extremities: Etiology, Classification and Treatment; Report of 300 cases, *Ann. Int. Med.* **9**:516 [Nov.] 1935.) In lymphedema it is usually possible to demonstrate some reduction in the size of the leg after the patient has been placed in bed, with the leg elevated to an angle of 30 degrees for forty-eight hours, but on account of the proliferating fibrosis in the superficial fascia the leg does not return to normal size, even after prolonged elevation. The only satisfactory treatment for lymphedema consists in the use of heavy elastic stockings or bandages, and operation of the Kondoleon type.

EFFECTS OF EXERCISE TEST ON EXTRASYSTOLES, MURMURS AND DIASTOLIC PRESSURE

To the Editor:—Kindly give your interpretation of the following in Queries and Minor Notes: Extrasystoles that do not disappear or even appear after the heart tolerance test, consisting of fifteen bends or twenty-five hops. Systolic murmurs that disappear in youth after the exercise test; also systolic murmurs, "no other heart findings," which disappear after exercise at the age of 40 or over, also drop in the systolic pressure after exercise test. It was stated that it is normal for the diastolic pressure to be elevated after the exercise test. My experience has been that it often drops even in young adults.

H. M. STRACHAN, M.D., Cleveland.

ANSWER.—Premature ventricular contractions will usually disappear during the exercise but reappear in the rest following the exercise. Occasionally, when not present before the exercise, they may appear in the rest after the exercise. Premature auricular contractions may follow a similar course or may appear after exercise and be more frequent after exercise and not disappear, or they may even first appear during exercise.

Systolic murmurs come and go with changes in tonus of the heart muscle or relative changes in different portions of the heart muscle. They may disappear after exertion as tonus increases or appear with conditions that decrease tonus, or because of the increased minute volume of blood passing through the valves.

Diastolic pressure usually follows the systolic and is usually more elevated following exercise. A fall in diastolic pressure after exercise has been assumed by some to be an index of myocardial damage. This may be true in some cases, but other normal physiologic factors may also be factors, and it is not safe to base an opinion on this alone.

AUSCULTATORY DETERMINATION OF BLOOD PRESSURE

To the Editor:—Will you please explain to me the following: In life insurance examinations with reference to blood pressure, I notice that they say diastolic fourth point and diastolic fifth point. Just what is meant by that?

JOSEPH HALTON, M.D., Sarasota, Fla.

ANSWER.—In the auscultatory determination of the arterial tension, five distinct phases of sound are heard. Each phase may vary considerably in duration and character, but the sequence is invariable. With inflation of the cuff to pressure above the systolic level, no sound is heard at the cubital fossa; but as the cuff is deflated one hears first sharp staccato clicks, which resemble normal cardiac sounds. This is the first phase, and the pressure at which these clicks appear is taken as the systolic pressure. The second phase is longer than the first and the sounds are best described as hissing or blowing murmurs. These arise because of whorls and eddies in the blood below the point of constriction. These sounds are transitory and disappear if constriction is maintained at this level of pressure. Occasionally, despite relatively rapid deflation, the sounds of the second phase disappear to cause the "auscultatory gap"; this phenomenon presumably occurs only in instances of hypertension and/or aortic stenosis. The transition to the third phase of sound is normally not sharply defined; the murmurs change to dull thuds, distinctly louder. The character of the thuds heard in the third phase varies with the condition of the arterial wall. When hypertonus of the artery exists and the walls are tense and rigid, the tones are louder than when the wall is relatively flaccid. The fourth phase appears when the thuds are abruptly muffled. The fourth phase is usually quite short and is soon followed by silence, which is the fifth point of change. Occasionally the fourth phase is prolonged and there is a considerable span between the appearance of muffling (fourth point) and silence (fifth point).

For many years the insurance companies were in the habit of requesting their examiners to determine the diastolic tension at the fifth point (in other words, at the disappearance of sound). However, it has been demonstrated repeatedly that this is incorrect. The true diastolic tension should be read at

the onset of the fourth phase, where the booming thuds are suddenly muffled. The average difference between these two points is about 5 mm. of mercury, but the error may be as much as 55 mm. As rating tables were based on the original fifth point diastolic tension, underwriters felt that the error was compensated for. It is wrong, nevertheless, to correct one error by introducing another. The present tendency of insurance medical directors to request both readings at the fourth and fifth points is to obtain figures for revision of their statistical data. The length of the fourth phase is variable and thus the error introduced by fifth point readings is inconstant. Just how inconstant this is can best be demonstrated by thousands of observations.

"C. N." DISINFECTANT AS INDUSTRIAL HAZARD

To the Editor:—I have recently had a case of gangrene of the fingers. This apparently occurred after exposure to a solution of C. N. in hot water. Would you kindly let me know the chemical composition of this product and whether there have been any case reports in the literature of gangrene following its use. Kindly omit name and address.

M.D., New York.

ANSWER.—C. N. is a coal tar disinfectant believed to be manufactured by the West Disinfecting Company and said to represent creosote containing aromatic hydrocarbons of double nucleus, the pyridine and chinoline bases, and the three isomeric cresols—ortho-, meta- and para-. Of the three cresols the ortho- and the para- are more toxic than phenol. Tricresol is a mixture of the isomeric cresols and is about nine-tenths as toxic as phenol. Saponated solution of cresol is a somewhat similar mixture of coal tar cresols along with soap solution. From the work of C. D. Harrington (THE JOURNAL, Feb. 13, 1909, p. 575) it may be recognized that the local effects of cresol are similar to those produced by phenol. Since phenol is well recognized as a source of gangrene, it is a tenable belief that cresols likewise may produce gangrene under conditions of appropriate exposure. Naturally, the probability of damage from cresols increases with the strength of the solution to which exposure is provided. Extensive discussion of the toxic properties of cresols (but without reference to C. N.) may be found in "Legal Medicine and Toxicology," by Peterson, Haines and Webster (ed. 2, Philadelphia, W. B. Saunders Company, 1926, second volume) and "Occupation and Health" (Geneva, International Labor Office, 1930, first volume).

EXOPHTHALMIC GOITER

To the Editor:—A girl of 16 is suffering from hyperthyroidism of probably a year's duration. The basal metabolism before treatment was plus 39 and after three weeks' bed rest, iodine therapy and ample diet was plus 17, with increase of weight from 109 to 121 pounds (49 to 55 Kg.) and improvement in well being, although nervousness, fatigue and emotional instability persist. The pulse at rest is 90. The heart shows no evidence of hypertrophy or impairment, although after an effort test the pulse failed to return to the previous rate in three minutes. The blood pressure remains 120 systolic, 72 diastolic. There is no evidence of other illness, except for a negative Wassermann reaction with plain antigen, 4 plus with cholesterinized antigen and 1 plus with the Kahn test. However, nothing in the history or examination tends to corroborate this observation. A thyroid specialist advises against roentgen therapy, as he says that results are too dubious and subsequent operation would be made very difficult as a result of fibrosis. Any advice you may give me as to my further handling of this case will be appreciated, especially as to the preference of irradiation or surgery. Kindly omit name.

M.D., New Jersey.

ANSWER.—The administration of iodine apparently does not eliminate the underlying factor responsible for exophthalmic goiter or primary hyperthyroidism, if one prefers so to designate this disease. Iodine, however, does control to a varying degree the symptoms of exophthalmic goiter. In a small proportion of cases it temporarily lowers the basal metabolic rate to within normal limits and for the time being completely eliminates the symptoms; later, in spite of the continued use of iodine, the basal metabolic rate returns to abnormally high levels and the symptoms recur. In a still smaller proportion of the cases, the basal metabolic rate remains within normal limits and the symptoms are completely controlled as long as the use of iodine is continued.

In those cases in which iodine either temporarily or permanently eliminates the symptoms, such complete control usually, but not always, results within two weeks following the institution of treatment. In the case described, however, iodine has not completely controlled the symptoms and the basal metabolic rate still is plus 17 per cent even though iodine has been administered for a period of three weeks. Furthermore, the rapid gain in weight that occurred in this case is not necessarily an indication that the disease is being controlled. In many cases of exophthalmic goiter, particularly in girls, a rapid gain in weight may occur during a period when the basal metabolic rate is very high and when the disease is progressing: the weight may reach a level that is well above the individual's normal weight.

If in this case the diagnosis is correct and the criteria are all as they appear to be, a partial thyroidectomy would seem to be the treatment of choice. This conclusion would be materially strengthened if palpation revealed that each lobe of the thyroid gland was sufficiently large to be readily grasped between the thumb and fingers of the examining hand and if the lobes were found to be relatively firm to palpation. The positive serologic tests in this case may be false positives. The case should be reconsidered from this angle, however, after the symptoms of exophthalmic goiter have subsided, in the course of from two to four months, and possibly an examination of the spinal fluid should be made.

MULTIPLE SCLEROSIS

To the Editor:—A white man, aged 32 years, fell down some steps eight years ago. He noted no ill effects at the time but two months later his right foot seemed to slap when walking. This sensation gradually changed to one in which the leg felt dead and dragged when he walked. There was no loss of sensation, pain, heat or position. He had no pain but had frequent cramps. In two months the condition passed suddenly and he had almost complete relief. Approximately every six months he has had similar attacks in the legs alternately. These attacks usually followed family arguments. During one of the early attacks he had a sensation of a "loose sack about his abdomen . . . as though his shirt were hanging out." He had difficulty in retaining his stool, which was normal in consistency and frequency. He had no urinary disturbances. The attacks are sudden in onset and last from three to four weeks. He has occasional attacks of tachycardia. The present attack (four weeks in duration) involves both legs and arms, which had never been involved before. The leg symptoms are similar to those described. In the arms there is a numb sensation from the elbows down. He feels that the hands are swollen. He has trouble picking up small objects, but there is no loss of grip or strength. Sensations of heat, cold and pain are unchanged. There is no pain. The abdomen feels as though it were overloaded. He has had numerous blood Wassermann tests, all of which proved negative. He refuses to have a spinal fluid examination. There is no history of venereal infection. His wife, two children, brothers and sisters are healthy. Physically he appears to be normal. There is a slight horizontal nystagmus but the other eye signs are normal. There is no muscular atrophy. The knee jerks are markedly exaggerated. There is a spurious ankle clonus. There is no intention tremor or past pointing. The Romberg sign is negative. The Babinski reflex is present. Sensation of heat, cold, pain and position are normal. The blood count and urine analysis are normal. I believe that this is a case of early multiple sclerosis. Do you believe the history and physical signs would confirm this diagnosis? Kindly suggest a course of treatment. Please omit name.

M.D., Pennsylvania.

ANSWER.—This may well be a case of multiple sclerosis. Are the abdominal reflexes absent in whole or in part? Normal abdominal reflexes are unusual in cases of multiple sclerosis of long standing. There are three methods of treatment now in vogue which have been shown to be effective in many cases and also to have failed in many cases. Consequently there is no generally accepted therapeutic method. The simplest one is the administration by mouth of quinine hydrochloride in capsules in doses of 0.3 Gm. three times a day over a period of years. Richard M. Brickner has written numerous articles on this treatment, one of the recent ones appearing in the *Archives of Neurology and Psychiatry* in June 1935. The second method worthy of trial is the giving two or three times a week of intravenous injections of sodium cacodylate in increasing doses up to 1 or 1.6 Gm. Such a course of a month or two may be given during periods of exacerbation in patients who receive the quinine treatment. The third method, which is more cumbersome, is fever therapy. At the present time the induction of fever by electricity is most popular, and there has been great improvement in technic and apparatus.

ABORTION FOR GONORRHEA AND TUBERCULOSIS

To the Editor:—Would there be any danger in performing a therapeutic abortion in a patient with a two months pregnancy, acute gonorrhea and a tuberculosis of three years' duration; if so, what? Would it be safe to do a curettage on this patient? She is 28 years old. Please omit name.

M.D., Chicago.

ANSWER.—There would, indeed, be the greatest possible danger in the performance of a therapeutic abortion in the presence of acute gonorrhea, and the safety of a curettage on this patient would be about the same as that of smoking a cigaret over an open keg of powder.

With the patient two months pregnant, the gonorrheal infection is at least limited to the vagina and cervix and can be

appropriately and effectively treated. An ill advised attempt at abortion would be almost certain to transform this into a gonorrheal metritis with parametritis and salpingitis.

Presumably the presence of tuberculosis in the patient in question has given rise to the thought by the correspondent that the pregnancy should be interrupted; assuredly this could not have been considered on account of the gonorrheal infection. Many authorities now maintain, with statistical evidence supporting their views, that pulmonary tuberculosis does not afford a valid reason for therapeutic abortion unless the patient's condition is becoming steadily worse. The latest editions of Williams' and of De Lee's textbooks discuss this in considerable detail.

ULCERATIVE COLITIS IN A CHILD

To the Editor:—I should like to know what regimen you would suggest in a case of so-called idiopathic ulcerative colitis in a child of 7½ years. The patient has been in bed for almost a year, the first four months of which was spent in a well recognized hospital where repeated stool examinations and cultures revealed no specific causative organism. Streptococcus viridans was found and an autogenous vaccine was made but therapy with this proved of no avail. The character of the stools (pus, mucus and blood) and the roentgenologic observations together with the objective symptoms make the diagnosis certain. A typical blood count consists of 4,000,000 red cells, 15,000 white cells and 60 per cent hemoglobin. The temperature range usually is from 98.6 to 100 daily. The weight (45 pounds, or 20 Kg.) and height (48 inches, or 122 cm.) have remained about stationary for the past year. The appetite is fair. The patient is confined to bed but would be up and around if allowed to be. There are no subjective symptoms except slight pain at stool. Colonic irrigations are painful and seem to aggravate the condition, as they are always followed by an increased amount of free bright red blood in the stools. The following therapeutic measures are being carried out: 1. General diet without roughage, vegetables being puréed or put through a sieve. No meat is swallowed. Meat juice is given daily. About 1 quart of milk is consumed daily and three quarts of coffee cream weekly. 2. Irradol-A thrice daily (4 cc.). 3 Calcium lactate by mouth (30 grains, or 2 Gm., daily). 4. Liver extract (Lilly's concentrated for parenteral use) 2 cc., injected into the gluteal muscles weekly. 5. Blood transfusions (from 100 to 200 cc. of whole blood) about every six weeks or two months by the multiple syringe method. This seems to give a boost each time. Specifically, what improvement can be expected by appendectomy or appendicostomy? Kindly omit name.

M.D., District of Columbia.

ANSWER.—Chronic ulcerative colitis is a severe destructive disease of the large intestine. It should be thought of much as one thinks of tuberculosis. The immediate prognosis in this disease when it attacks a child in the first decade is not good, but slow progressive improvement usually occurs. This may take from months to years but, as a rule, unless acute recurrent infection intervenes, gradual healing of the process will usually occur under the following regimen: a generous high calory, high protein and low residue type of diet, occasional small blood transfusions, sedatives and powders as indicated, and anticolitis serum given at intervals followed by the administration of vaccine from the organisms isolated from the rectal lesions. The injections of the serum and vaccine should be continued periodically for many months. Occasionally some improvement occurs following appendicostomy, but, if surgery becomes advisable, ileostomy is the preferable procedure. Either one of these procedures may be followed by such narrowing of the bowel that the stoma may have to be a permanent one. In a child of 7½ years this is undesirable.

TWIN PREGNANCY WITH DEATH OF ONE FETUS

To the Editor:—There is a question in a recent issue of THE JOURNAL (Nov. 7, 1936, p. 1583) pertaining to twin pregnancies in which one fetus died at some time previous to the delivery of a living fetus. A similar case has recently been observed except that at about three and one-half months there was premature rupture of the membrane surrounding one fetus. An x-ray diagnosis of twins was made. The patient was very desirous of having a child and the question arose as to the possibility of her carrying the other fetus along to a viable age. The patient promptly aborted both fetuses. Can you tell me whether there is any case on record of premature rupture of membranes in a twin pregnancy at a time before viability of the fetus and subsequent growth of one or both fetuses to age of viability? Please omit name.

M.D., California.

ANSWER.—Multiple pregnancy is probably more common than the recorded literature would indicate. A fetus papyraceus or compressus might be missed if the placenta and secundines are examined too carelessly. In double ovum twins, one fetus may die and be expelled, the other going normally to term. Thus M. G. Burris delivered a living female infant weighing 7 pounds (3.2 Kg.) from a woman who gave a history of having passed a fetus 3 inches long with placenta and cord attached in the third month of the same pregnancy. (Burris, M. G.: *Canad. M. A. J.* **16**:170 [Feb.] 1926.)

De Lee delivered a woman at term of twins who stated that five months previously she had had an abortion of four months (De Lee, J. B.: Principles and Practice of Obstetrics, 1936, p. 513). Dr. T. J. Watkins (quoted by De Lee) relates the case of the delivery of twins at three months and triplets at term of the same pregnancy. Early death of one fetus may not alway be followed by abortion even though the fetus becomes macerated. T. J. Parks (*Am. J. Obst. & Gynec.* **21**:112 [Jan.] 1931) reports the delivery of a 1,772 Gm. fetus, 43 cm. long, in a monochorionic twin pregnancy. The other fetus was small and macerated, and both amniotic sacs were found ruptured at the time of delivery. Other cases also have been reported. When abortion of twins occurs there may even be an interval of several months between the expulsion of the first and the second fetus, as in the case cited by G. H. Schneider (*Monatschr. f. Geburtsh. u. Gynäk.* **73**:5 [April] 1926).

ICTERUS DURING TREATMENT FOR SYPHILIS

To the Editor:—A patient was seen Sept. 4, 1936, with a primary chancre of syphilis and a 4 plus Wassermann reaction. He has received six injections of neoarsphenamine (dosage 0.6 Gm. September 8, 11, 14, 21, 28 and October 4). In addition on September 8 and 11 he received two injections of bismuth salicylate 2 grains (0.13 Gm.). Four days after the last injection of neoarsphenamine he presented himself with marked jaundice and bile in the urine. He is symptom free, as the chancre has healed, and he has never had a secondary eruption. I would appreciate your advice as to the proper drugs to use in future treatment; in other words, I would like to have a full outline as to the method of conducting treatment in face of the jaundice. The urine examination is negative. I have not done a spinal tap as yet. Please omit name if published.

M.D., New York.

ANSWER.—Icterus occurring during the course of early syphilis under treatment with the arsphenamines is by no means infrequent. It has been variously interpreted as being due to the syphilitic virus, in other words an early syphilitic hepatitis, and as being caused by the arsphenamines, owing to their destructive effect on the spirochetes in the liver. Still others, Stokes in particular, look on it as an epidemic catarrhal jaundice complicating syphilis therapy. It has also been suggested that the icterus is due to a hepatic localization of the Herxheimer reaction.

Whatever the explanation, when icterus develops during arsphenamine therapy it is wiser to discontinue the arsenical injections and give a few doses of sodium thiosulfate (1 Gm.) every other day intravenously. The diet should be a low fat, high carbohydrate diet and in severe cases hypertonic dextrose should be given intravenously in doses of from 25 to 50 cc. of a 50 per cent solution. As soon as the icterus has subsided, treatment should be cautiously resumed with bismuth preparations. Determinations of the bilirubin content of the blood by means of the van den Bergh reaction and the icterus index should be used as controls.

Milian is practically the only author who advises a continuation of arsphenamine therapy in cases of jaundice on the assumption that it is of syphilitic origin.

The danger of a possible acute yellow atrophy of the liver should be kept in mind.

AURICULAR FIBRILLATION

To the Editor:—A woman, aged 42, was seen by me after a three day illness complaining of marked palpitation. The heart rate was over 200 but regular. There was no objective or subjective evidence of cardiac decompensation. The blood pressure was 120 systolic, 80 diastolic. After rest, sedatives and quinidine in 6 grain (0.4 Gm.) doses daily the heart rate slowed down to 100 but is totally irregular. Use of digitalis with subsequent quinidine administration and administration of the two together has failed to correct the auricular fibrillation (which I presume it is). There is present a mitral systolic murmur. The heart is not enlarged by percussion. The patient is comfortable. The patient was examined eight years ago and passed for life insurance and has had no illnesses or any rheumatic manifestation. The basal metabolic rate is plus 6. What is the cause of the irregularity? Is digitalis indicated? What can be done to correct the cardiac irregularity? Kindly omit name.

M.D., New York.

ANSWER.—The onset of auricular fibrillation may be preceded by rapid, regular pulse. An auricular fibrillation with a rate of 200 may appear regular. Digitalis is indicated only to control the rate of the heart and to maintain the heart rate at a level that gives the best clinical response.

An attempt can be made to restore the heart to a normal mechanism by means of quinidine, or the rate can be controlled indefinitely by means of digitalis in proper dosage. It is not so much the auricular fibrillation that is a mechanical deterrent as it is the rapid rate which accompanies it and which results in a decreased minute volume of blood being delivered by the heart.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Juneau.

ARIZONA: Phoenix, Jan. 5-6. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

CALIFORNIA: *Reciprocity.* San Francisco, Jan. 6. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, Jan. 5. Sec., Dr. Harvey W. Snyder, 422 State Office Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 13. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven. *Medical (Homeopathic).* Derby, Feb. 13. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven. *Medical (Regular).* Hartford, March 9-10. *Endorsement.* Hartford, March 23. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden.

DISTRICT OF COLUMBIA: Washington, Jan. 11-12. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

IDAHO: Boise, April 6. Commissioner of Law Enforcement, Hon. Emmitt Pfost, 205 State House, Boise.

ILLINOIS: Chicago, Jan. 26-28. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 22-24. Sec., Board of Medical Registration and Examination, Dr. William R. Davidson, 301 State House, Indianapolis.

IOWA: *Basic Science.* Des Moines, Jan. 12. Sec., Prof. Edward A. Benbrook, Iowa State College, Ames.

MAINE: Portland, March 9-10. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 5-6. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, Jan. 19-21. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MONTANA: Helena, April 6. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.

NEBRASKA: *Basic Science.* Omaha, Jan. 12-13. Director, Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: *Reciprocity.* Carson City, Feb. 1. Sec., Dr. John E. Worden, Carson City.

NEW HAMPSHIRE: Concord, March 11-12. Sec., Board of Registration in Medicine, Dr. Charles Duncan, State House, Concord.

NEW MEXICO: Santa Fe, April 12-13. Sec., Dr. Le Grand Ward, Box 693, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 25-28. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 5-8. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OREGON: Portland, Jan. 5-7. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland.

PENNSYLVANIA: Philadelphia, Jan. 5-9. Sec., Board of Medical Education and Licensure, Mr. James A. Newpher, Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 2. Sec., Dr. O. Costa Mandry, Box 536, San Juan.

RHODE ISLAND: Providence, Jan. 7-8. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 19-20. Dir., Division of Medical Licensure, Dr. B. A. Dyar, Pierre.

VERMONT: Burlington, Feb. 10-12. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WASHINGTON: *Basic Science.* Seattle, Jan. 7-8. *Medical.* Seattle, Jan. 11-13. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

WEST VIRGINIA: Charleston, March 1. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 12-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Feb. 1. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Feb. 9-11, May 10-12, June 21-23, and Sept. 13-15. *Part III.* New York, Jan. 11-13 and Chicago, Jan. 19-21. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF INTERNAL MEDICINE: *Written* examination will be held simultaneously in different centers of the United States and Canada in March. *Practical* examination will be given in St. Louis in April and at Philadelphia in June. Chairman, Dr. Walter L. Bierring, 406 Sixth Ave., Rm. 1210, Des Moines.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examination for Group B applicants* will be held in various cities throughout the United States and Canada, March 6. *Practical, oral and clinical examinations for Group A and B applicants* will be held at Atlantic City, N. J., June 7-8. *Applications must be received at least sixty days prior to the examination dates.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: Los Angeles, Jan. 23. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Cleveland, Jan. 9. Sec., Dr. Fremont A. Chandler, 180 N. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Philadelphia, June 7-8. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Chicago, March 26-27. Sec., Dr. F. W. Hartman, Henry Ford Hosital, Detroit, Michigan.

AMERICAN BOARD OF PEDIATRICS: New York, Jan. 23. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Illinois.

West Virginia October Report

Dr. Arthur E. McClue, secretary, West Virginia Public Health Council, reports the oral and written examination held in Wheeling, Oct. 12-14, 1936. The examination covered 11 subjects and included 110 questions. An average of 80 per cent was required to pass. Fourteen candidates were examined, all of whom passed. Nine physicians were licensed by reciprocity and 1 physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Howard University College of Medicine		(1935)	87.8
Northwestern University Medical School		(1935)	89.3
New York University, University and Bellevue Hospital Medical College		(1934)	90.8
Duke University School of Medicine		(1933)	85.1
University of Cincinnati College of Medicine		(1935)	85.3
Hahnemann Medical College and Hosp. of Philadelphia		(1935)	84.1
Jefferson Medical College of Philadelphia		(1935)	87.8, 90.7
Medical College of Virginia		(1934) 88.2, (1935)	86.3, 87.2
University of Virginia Department of Medicine		(1928) (1934) 89.6, (1935) 83.7	88.3,

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Maryland School of Medicine and College of Physicians and Surgeons		(1935)	Maryland
University of Michigan Medical School		(1932)	Penna.
Washington University School of Medicine		(1934)	Missouri
Ohio-Miami Medical College		(1913)	Ohio
Western Reserve University School of Medicine		(1933)	Ohio
University of Oklahoma School of Medicine		(1935)	Oklahoma
Temple University School of Medicine		(1934)	Penna.
Medical College of Virginia		(1911)	Virginia
University of Virginia Department of Medicine		(1932)	Virginia

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard University Medical School		(1934)	N. B. M. Ex.

Wisconsin Reciprocity Report

Dr. Henry J. Gramling, secretary, Wisconsin State Board of Medical Examiners, reports 11 applicants licensed by reciprocity at the meeting held at Madison, September 8, 1936. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Loyola University School of Medicine		(1932)	Illinois
Indiana University School of Medicine		(1930)	Indiana
State University of Iowa College of Medicine		(1932)	Iowa
University of Louisville School of Medicine		(1934)	Minnesota
Tulane University of Louisiana School of Medicine		(1915)	Louisiana
University of Minnesota Medical School		(1930), (1935)	Minnesota
Columbia University College of Physicians and Surgeons		(1932)	New York
Ohio State University College of Medicine		(1931)	Ohio
University of Wisconsin Medical School		(1927)	Michigan
Osteopath*			Illinois

* Licensed to practice osteopathy and surgery.

Indiana June Examination

Dr. William R. Davidson, secretary, Indiana State Board of Medical Registration and Examination, reports the written examination held in Indianapolis, June 23-25, 1936. The examination covered 15 subjects and included 100 questions. One hundred and eighteen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent.
Loyola University School of Medicine		(1936, 5),* (1936)	84.9
University of Illinois College of Medicine		(1934)	82.4
Indiana University School of Medicine		(1935)	85.2, 85.9, (1936) 78.7, 79.2, 79.7, 79.7, 79.9, 80, 80, 80, 80, 80.2, 80.2, 80.3, 80.5, 80.6, 80.6, 80.7, 80.8, 80.8, 80.9, 80.9, 81.1, 81.1, 81.2, 81.2, 81.2, 81.4, 81.4, 81.4, 81.4, 81.4, 81.5, 81.5, 81.6, 81.6, 81.8, 81.8, 81.9, 81.9, 82, 82.1, 82.1, 82.1, 82.1, 82.3, 82.3, 82.3, 82.4, 82.5, 82.5, 82.6, 82.7, 82.7, 82.8, 82.8, 82.9, 82.9, 83, 83.1, 83.1, 83.2, 83.2, 83.2, 83.4, 83.4, 83.4, 83.5, 83.5, 83.7, 83.9, 84.1, 84.1, 84.2, 84.4, 84.4, 84.5, 84.5, 84.5, 84.6, 84.7, 84.7, 85.4, 85.5, 85.6, 85.6, 85.6, 85.6, 85.8, 85.8, 85.9, 86, 86, 86.3, 86.3, 86.3, 86.6, 86.6, 87.5, 87.7, 87.9, 90.4,†
University of Kansas School of Medicine		(1933)	84.3
Tulane University of Louisiana School of Medicine		(1935)	85.5
St. Louis University School of Medicine		(1936)	82.9
Ohio State University College of Medicine		(1931)	82.6
Marquette University School of Medicine		(1936)	82.6, 83.8
Queen's University Faculty of Medicine		(1936)	84.9

* These applicants have completed the medical course and will receive the M.D. degree on completion of internship. Licenses have not been issued.

† This applicant has not received diploma, taking two years to complete senior work. License has not been issued.

Book Notices

A Text-Book of Pharmacology and Therapeutics or the Action of Drugs in Health and Disease. By Arthur R. Cushny, M.A., M.D., LL.D. Eleventh edition, revised by C. W. Edmunds, A.B., M.D., Professor of Materia Medica and Therapeutics and Director of the Pharmacological Laboratories in the University of Michigan, Ann Arbor, and J. A. Gunn, M.A., M.D., D.Sc., Professor of Pharmacology and Director of the Nuffield Institute for Medical Research, University of Oxford, Oxford, England. Cloth. Price, $6.50. Pp. 808, with 70 illustrations. Philadelphia: Lea & Febiger, 1936.

To keep a textbook on pharmacology down to date requires arduous work on the part of the authors. Not only must the authors be abreast of the increasing fund of knowledge related to drugs and their actions but the book must be brought into conformity with the ever changing standards of official compendiums such as the U. S. Pharmacopeia and the British Pharmacopeia. Since the decennial revisions of official books of standards became official this year, nearly every book dealing with official medicaments has undergone a revision. Cushny's Pharmacology and Therapeutics by Edmunds and Gunn is subject to increasing watchfulness because it covers not only the drugs of the United States but those standardized in the British empire. The 1936 revision has been thorough. Not only has the text been revised but there has been a noticeable rearrangement of the order of the book and discussions of the subjects. In this arrangement the idea has been that the simpler substances should be discussed first, leaving the more complex considerations toward the latter part of the book, though no didactic rule could be made. In common with most pharmacologies, it is necessary to have an introduction to the field of pharmacology and its definitions so that the student or consultant may interpret better the technical discussions.

To one who has followed the development of textbooks on pharmacology it is noted that therapeutics has been changing, particularly in the last few years, by intensive study of those extremely active substances which are loosely classified as vitamins, hormones or glandular principles. Twenty years ago almost no mention was made of liver and liver preparations; today they form an important part of materia medica. The same is true of the vitamins, which require approximately fourteen pages for a limited discussion by Edmunds and Gunn. Also noticeable is the much better understanding of glandular therapy today, as is evidenced by the technical discussions in pharmacologies. And yet these discussions cannot help but be simply epitomizations of the knowledge that is required for scientific clinical practice.

A particularly valuable discussion by the authors is that on the opium series. Space does not permit critical comment of many of the excellent chapters contained in this book. There is, however, one criticism to be made—the index is hardly ample for a book containing as much useful information as Cushny's Pharmacology. In accord with previous editions, the book is printed on excellent paper and the typographical setup is inviting. The bibliographies of the discussions, while ample, are not extensive. The book is one that will continue to receive recognition both in Great Britain and in the United States.

Techniques chirurgicales. Publiées par A. Gosset, chirurgien de la Salpêtrière. Avec la collaboration de L. G. Amiot, et al. Cloth. Price, 125 francs. Pp. 436, with 22 illustrations. Paris: Masson & Cie, 1936.

Of late there has been a tendency to group the works of many under the editorship of one individual. Gosset assumes such a rôle in this work. The book is divided into fifteen chapters. While it is not a manual for the student, it affords excellent reading for the experienced surgeon. Gosset's collaborators work at the Salpêtrière, where he has been director for the last twenty years. Much space is devoted to organization and hospital methods, sterilization, equipment, architecture of the pathologic and anatomic laboratories, the library and the operating room. It concludes with a roster of the surgeons and their assistants. It also carries the announcement that Dr. Le Noir, member of the Academy of Medicine and honorary physician of the hospitals, conducts in Gosset's service consultations in gastro-enterology, "meticulously carried out." Custom and taste obviously differ among men of science in various habitats. A great deal of space (more than a hundred pages) is devoted to the details of sterilization and the biochemistry of anesthesia.

Petit-Dutaillis contributes a chapter on neurotomy of the trigeminus through a posterior approach, which is written lucidly and is illuminatingly illustrated by Frantz, who created for himself an enviable reputation as a medical illustrator. His fine work is in decided contrast to the photography in the preliminary chapters, which is rather inferior. Sauvage and Wallon point out, as the result of an intensive study, that a combination of surgery and radium in cases of cancer affecting the upper jaw is effective, if attacked early. They stress the importance of early diagnosis and counsel that serious consideration be given to such apparently simple manifestations as nasal discharge, toothache and persistent sinusitis, which may all be telltale symptoms of an early carcinoma of that region. In their series of cases (many were desperate) they were able to observe successful results from three to ten years in nine instances. "If that is so," ask the authors, "how much better results may one expect in cases which are diagnosed early and promptly subjected to treatment." Soupault (chapter 7) discusses diaphragmatic hernia but offers nothing of a departure from the standard methods now in vogue. Charrier (chapter 8) describes gastrectomy as related to gastrojejunal ulcer. It is well illustrated, as is the succeeding chapter on gastrectomy for carcinoma by Georges Loewy. Gosset contributes chapter 10, on appendicitis. He uses the McBurney incision, which in certain quarters in England is being abandoned in favor of the pararectus approach. Gosset discusses indications for operative intervention in an excellent manner. He stresses what he stressed some thirty years ago: "My formula is simple," says Gosset; "operate always and operate promptly." He has no patience with procrastination, no matter under what form. Where expectancy seems indicated, his advice recalls the aphorism of Hamilton Bailey to "practice expectancy at the door of the operating theater." Again while the pendulum is still swinging on the question whether to drain or not to drain in appendicitis, Gosset justly reminds us that there exists no universal formula—that cases for drainage or those not to be drained must be selected; yet in every case of doubt "I drain," says Gosset, adding "What disadvantages can there come from drainage? These are certainly minor, but in certain cases the absence of a drain may spell death." To this dictum one may wholeheartedly subscribe. Another advantage of drainage, in the sense of Gosset, besides permitting septic material to find its way to the surface, is that the opening through which the drain emerges may be used to introduce antigangrenous and anticolibacillary serum, which when introduced intramuscularly are not as effective as when injected through the opening created by the drain. In cases of diffuse peritonitis, Gosset counsels counter drainage through the left iliac fossa; he reminds us that, in the iliac forms of appendicitis attended by much suppuration and operated on late, "one cannot always present the patient with the appendix." This chapter concludes with the treatment of right inguinal hernia with complementary appendectomy.

Intestinal obstruction, to which surgeons are paying much just attention of late, is ably discussed by Ledoux-Lebard, Thalheimer and Garcia-Calderon. These authors stress the importance of early diagnosis and depend mainly on radioscopy and the barium sulfate enema for the localization of the seat of obstruction. The chapter is illustrated by roentgenograms and concludes with indications for operative intervention. No mention is made of abdominal auscultation, so important a diagnostic medium according to certain American surgeons. Carcinoma of the large bowel claims the greater part of the remaining text. Right hemicolectomy is discussed by Gosset and illustrated by Frantz; carcinoma of the left colon is discussed by Ledoux-Lebard. In English literature exteriorization procedures are usually credited to Paul-Mikulicz; here Bloch's name is substituted for that of Paul. It seems that Bloch has preceded Paul in the thought of exteriorization of the bowel in carcinoma of the left colon, while Mikulicz, according to the late Lord Moynihan, contributed nothing original to the subject other than elaborating on the ideas of his predecessors. Fred Rankin is justly mentioned with reference to some technical details connected with operations on carcinoma of the colon. The importance of cecostomy is

stressed. The description of the procedure is graphic, thorough and painstaking. The illustrations are equally good. A clamp applied to the cecum to avoid soiling, while mentioned in the text, is not shown in the illustration; while this is not a serious omission to the advanced surgeon, it certainly is of utmost importance for the beginner. The other steps of the operation are well illustrated. The final chapters are devoted to a discussion on the results obtained from treating fibroids of the uterus surgically by Gosset and Funck-Brentano, and the treatment of complicated fractures of the ankle, by Guy Seille. A bibliography is attached to each chapter.

Skyways to a Jungle Laboratory: An African Adventure. By Grace Crile. Cloth. Price, $2.75. Pp. 240, with 51 illustrations. New York: W. W. Norton & Company, Inc., 1936.

Mrs. Crile describes the journey from London to Nairobi by Imperial Airways—except from Paris to Brindisi—and adventures in connection with a "jungle" laboratory situated "in the richest territory in the world for abundance and variety of animal life." The first fifty pages are concerned with the journey to Nairobi and are replete with information on the country covered. The author, an intelligent observer, knows what she sees, whether on land or water, so that her descriptions are both interesting and informing. The journey from London to Khartoum may be regarded as within the borders of civilization, since Khartoum can be reached by rail and is attracting tourists. But what of the trip from Khartoum to Nairobi through much of darkest Africa? It took two days and a night. What about food and sleep? A few quotations will answer the questions:

Malakal: From the Grand Hotel at Khartoum "the plane was off at 6:40 a. m. . . . reached Malakal at 10:30. . . . The tall native chief broke a hole in each petrol tin with a big ugly knife, natives swarmed around to watch, and we were refueled. Meanwhile we were invited into a cool, screened tent for lunch. Here tables were spread and delicious Nile fish, potatoes, beans, a compote of mixed canned fruit and coffee were served on pretty Airways china. This is England—off at the end of nowhere."

Juba for the night: "We arrived at Juba about 3 o'clock in time for tea on the veranda. . . . The bedrooms were prettily furnished . . . each has a screened porch . . . electric fan. We luxuriated in hot baths. . . . During dinner a radio played in the next room and we heard quotations of the various stockmarkets, so we are not so far away from everywhere after all."

Entebbe: "It was still dark when we climbed into the plane (at Juba) with promise of breakfast at Entebbe some 340 miles on. . . . We breakfasted at nine on luscious pineapple, the best little finger-long bananas I ever ate, bacon, eggs, sausages and coffee. The hotel was clean and attractive."

Kisumu: "We stopped at Kisumu for breakfast. Apparently everything one plants at Kisumu grows. There were flowers of the most gorgeous hues all around the hotel."

As Nairobi is reached in two or three hours after one leaves Kisumu it is quite evident that "Skyways" over Africa entails no hardships; rather it would seem that this would be a fine pleasure trip. From Nairobi to "Journeys end," which means Maji Moto Camp, was by plane and automobile. "Maji Moto Camp consists of fourteen native huts built of mud, reed and bamboo, and thatched with straw, encircling a large ring where the fire burns at night and two boys stand guard. We are 3½ degrees south of the equator. The altitude is about 4,000 feet. Here night falls like a curtain. At five minutes of six it is light. At five minutes past six it is night." One of these huts became the "Jungle Laboratory." The staff consisted of Dr. and Mrs. Crile; Daniel P. Quiring, Ph.D., of the department of biology of Western Reserve University; A. B. Fuller, chief preparator of the Cleveland Museum of Natural History; Dr. W. H. Carr, a young English physician who went out to hunt but joined the group and assisted in the dissections; Bryan Cooper, a biologist, and Captain J. R. Hewett. In the division of the work Mrs. Crile was allotted the task to "weigh the organs and keep the records."

Animals dissected ranged from the elephant, rhino and hippo down to the innocent little dik dik. Of course it was necessary to catch and kill the animal before it could be dissected. Here is where the sport came in—a sport which supplied plenty of adventures and not a little danger. These, the adventures and dangers, the author has here recorded in a manner which, if equaled by her records of the dissections, will make the latter delightful reading. One hundred and fifty original photographs, many in group pictures, practically all taken by members of the staff, add interest and value to the book.

Pédiatrie pratique. Répertoire de mises au point. Indications et moyens thérapeutiques. Par Eugène Terrien. Paper. Price, 24 francs. Pp. 247. Paris: Masson & Cie, 1936.

This paper bound volume is in no sense a textbook, being more a brief outline of methods of treatment recently employed in the various ailments of children. The diseases or syndromes are arranged in alphabetical order. Usually little more than a page is given to any particular disorder, the discussion being limited to a brief description of the nature of the disease, occasionally a word as to its etiology or symptomatology, one or more brief paragraphs on treatment, usually including suggestions from a number of writers, and finally a terse conclusion. Some of the treatment recommended varies considerably from that employed in this country. In acrodynia, acetylcholine and the x-rays are recommended. In adiposogenital dystrophy, antisyphilitic treatment has at times been highly successful. In severe tonsillitis and pharyngitis, irrigation of the throat with seltzer water gives relief. For the practitioner of pediatrics, the book has some value. Its convenient arrangement and form as well as its brief but definite suggestions make it a concise little guide. The busy practitioner may in a few moments review the newest ideas in treatment and may at times find methods that are new to him.

A Text-Book of Physiology. By H. E. Roaf, M.D., D.Sc., M.R.C.S., Professor of Physiology in the University of Liverpool. Second edition. Cloth. Price, $6.75. Pp. 679, with 338 illustrations. Baltimore: William Wood & Company, 1936.

This book is meant for medical students and others taking a first comprehensive course in physiology. As such it is a reasonably satisfactory work. It treats all the major fields of the subject and gives a great deal of information, though not always with a great deal of critical acumen. For example, it is stated categorically, and a chemical equation is written purporting to show, that the gastric hydrochloric acid is derived from a reaction between sodium chloride and carbonic acid.

A beginning student could scarcely be blamed for interpreting that statement literally. Another example of this type of defect appears in the last chapter, on emotional reactions. Here the ideology of psychoanalysis is freely, and without critical comment, incorporated as physiologic dogma. The assumption, for example, of a "censor" for an extensive subconscious mind is not based on acceptable scientific data and does not deserve unqualified acceptance in a teaching textbook of physiology. Other unjustifiable tacit assumptions greatly detract from the value of this portion of the book, although it must be admitted that the incorporation of some experimental psychology is in itself a real asset. These criticisms should not be taken to imply that there are not valuable sections in the book. The first chapter gives an excellent elementary account of the mechanics of posture and movement.

New and Nonofficial Remedies, 1936, Containing Descriptions of the Articles Which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1936. Cloth. Price, $1.50. Pp. 542. Chicago: American Medical Association, 1936.

The appearance of the U. S. P. XI made necessary an extensive revision of the 1936 edition of New and Nonofficial Remedies. This seems somewhat paradoxical in view of the name of the Council's valuable book. But the fact is that there have always been included in New and Nonofficial Remedies a great many official drugs. Manufacturers apparently have appreciated the distinction given their brands by Council acceptance, and the public and the medical profession have certainly benefited by the Council's supervision of advertising claims for products the fundamental value of which has already been established. Of the fifty-four therapeutic agents added to the Pharmacopeia, forty-one as nonofficial preparations stood accepted for New and Nonofficial Remedies. The following is a list of the former N. N. R. preparations that are now official in the Pharmacopeia (the new pharmacopeial name is given): Acriflavine, Acriflavine Hydrochloride, Ethylene, Ethylhydrocupreine Hydrochloride, Scarlet Fever Antitoxin, Bismuth and Potassium Tartrate, Calcium Creosotate, Calcium Gluconate, Chlorbutanol, Emulsion of Liquid Petrolatum, Ephedrine, Ephedrine Hydrochloride, Ephedrine Sulfate, Diluted Erythrityl Tetranitrate, Extract of Liver, Green Iron and Ammonium Citrates, Soluble Fluorescein, Mercuric Succinimide, Iodo-

phthalein, Solution of Irradiated Ergosterol, Solution of Liver, Purified Solution of Liver, Solution of Parathyroid, Merbaphen, Neocincophen, Iodized Oil, Phenacaine Hydrochloride, Soluble Phenobarbital, Chiniofon Powder, Antimeningococcic Serum, Antipneumococcic Serum, Type I, Stomach, Theophylline with Ethylene Diamine, Theophylline with Sodium Acetate, Diphtheria Toxoid, Diphtheria Toxin for the Schick Test, Scarlet Fever Streptococcus Toxin, Tryparsamide, Old Tuberculin, Rabies Vaccine, Bacterial Vaccine made from the Typhoid Bacillus, Bacterial Vaccine made from Typhoid Bacillus and the Paratyphoid A and B Bacilli.

In most cases the New and Nonofficial Remedies tests and standards were taken over in whole or in part by the Pharmacopeia. This is eloquent evidence of the wisdom of the Council's selections since the appearance of the U. S. P. X.

Among the new products described in this edition of New and Nonofficial Remedies are Isopropyl Alcohol, Aminoacetic Acid, Larocaine Hydrochloride, Alurate and Sodium Alurate, Ipral Sodium, Ephedrine Hemihydrate, Azochloramid, Beta-Lactose, Pyrethrum Ointment, Meningococcus Antitoxin and Staphylococcus Toxoid.

Noteworthy revisions have been made of the chapters on Bismuth Compounds, Organs of Animals and Serums and Vaccines. These annual revisions place each succeeding edition of New and Nonofficial Remedies in a class by itself as an authoritative guide to therapeutic progress.

Sport- und Arbeitsschäden: Eine Zusammenfassung klinischer Beobachtungen und wissenschaftlicher Erkenntnisse zur Biologie der Arbeit und Pathologie der Funktion. Von Wilhelm Baetzner, Direktor der 3. Chirurgischen Universitätsklinik im Städtischen Robert-Koch-Krankenhaus, Berlin. Mit einem Geleitwort von Professor August Bier. Im Jahre der XI. Olympischen Spiele 1936. Paper. Price, 8 marks. Pp. 136, with 133 illustrations. Leipzig: Georg Thieme, 1936.

The theme of this book is that sports should be used to strengthen and develop the body, as one might use medicine, and not overdone for the sake of records that demand using the last strength with the last breath. In Germany there is a tendency to overemphasize athletics for the sake of making new records and winning contests, as notably the Olympic games. Overtraining and overexertion are a detriment to physical development and well being. Generalized sports are not good for every one. Sports demand motions foreign to joints and organs. Athletic injuries are similar to industrial injuries, but the latter never demand overstrain except in the continued use of one set of muscles in certain types of work. Athletes are more prone to infection and their cuts, bruises and injured bones do not heal so well as other injuries. Athletes are often poor workers and cannot do good brain work when exercising too much. Hard exercise depresses the glandular activity and lessens the birth rate. A woman active in sport rarely brings up a child, and males have fewer offspring. Champion athletes, e. g., Cambridge and Oxford oarsmen, usually do not amount to much in life, are weak and die early. Pneumonia kills many athletes. Hypertrophied organs disturb the mutual relation of the organs. The proper athletics should be good for every one and not be reserved for a privileged class of good athletes. Properly indulged in, sports should improve the general health. Severe recreational exercise should not be combined with heavy work, but a brain worker should take up a sport. Critics have attacked this theory, especially coaches and athletes. A habitual athlete receives severe injuries as a result of his overactivity. Many so-called injuries are the result of damage from prolonged indulgence or overstrain. The author cites many illustrations of these injuries, including a javelin thrower whose humerus fractured while throwing, and a football player who fractured his femur while in the air. Tabler quotes observations on 1,400 Swiss mountaineers in whom injuries to the meniscus showed premature degeneration due to abnormal use of knees in the mountains. Many joints showing degenerative and proliferative changes, loose bodies and spurs are cited. Osteochondritis dissecans is shown in the knee, hand, wrist, foot, ischium and elbow. Bone changes occur, fractures, osteoporosis, split patellae, degenerative changes as in tibial tubercle, the navicular bone, the metatarsals, split fibulae and osseous proliferation. Injuries in the muscles, tendons and ligaments are illustrated. The illustrations are excellent, showing a great variety of roentgenograms illustrating the different lesions. The book is well written and typically German in that it takes up the etiology and pathology rather exhaustively and says practically nothing about treatment. The multiplicity of examples and the redundant repetition of the main theme are calculated to impress the point on even the most ponderous of Teutonic intellects.

Materia Medica and Therapeutics: A Text-Book for Nurses. By Linette A. Parker, B.Sc., R.N. Sixth edition. Cloth. Price, $2.50. Pp. 377, with 35 illustrations. Philadelphia: Lea & Febiger, 1936.

In a book that gives so much that is practical in so small a space, much has to be forgiven. There is no doubt that it fills the needs for which it is designed as well as and perhaps better than some other books on the subject. It would be desirable, however, if a person who teaches this subject and especially one who writes on it were somewhat better grounded in pharmacology than the author seems to be. Thus to mention strychnine as a true heart stimulant or to consider morphine and bromides as heart depressants is not in line with modern teaching. However, it probably does not do much harm, as professional ethics requires nurses to receive opinions respectfully on the action of drugs expressed by doctors who are not much better grounded in their knowledge of pharmacology.

Fundamentals of Human Physiology. By the late J. J. R. MacLeod, M.B., D.Sc., F.R.S., and R. J. Seymour, M.S., M.D., Professor of Physiology, Ohio State University, Columbus, Ohio. Fourth edition. Cloth. Price, $2.50. Pp. 424, with 108 illustrations. St. Louis: C. V. Mosby Company, 1936.

This first venture into the field of authorship by a man whose major interest for many years has been the teaching of elementary physiology to college students is a well arranged and constructed textbook in which the good features of earlier editions have been retained and amplified on the basis of the author's experience in this particular field. Experience in teaching elementary physiology motivates a general criticism, which applies to most elementary textbooks on physiology; namely, too great a degree of attenuation of factual material and too little effort to apply facts to everyday life. A student in a course to which this textbook is applicable will in most instances never go any further in the study of physiology. It is all the more important, therefore, that every possible application be made to circumstances of living. This textbook fails largely to accomplish this end except in a brief appendix on public and personal hygiene devoted to communicable diseases, industrial hygiene, sewage disposal, water and food, hygiene of excretion, ventilation, hygiene of the nervous and muscular systems and child hygiene, but the discussion is too brief even to stimulate the student to further inquiry. There is an excellent glossary of physiologic terms, which should be a valuable aid to the beginning student. Some of the illustrations are poorly reproduced, such as figures 28, 42, 43, 45, 46, 64, 65, 66, 67, 68, 69, 70 and 89; pen drawings, color plates and diagrams are, however, well reproduced and are in general well selected. The sections on endocrines and vitamins are inadequate as to both content and presentation. The revising author has to a considerable degree failed to take advantage of an opportunity to make the subject of physiology live for the most eager and enthusiastic class of students of the subject, namely, those who elect to take the course for the sake of their own general enlightenment.

Fisiopatologia della ghiandola pineale. Dal Dott. Francesco Molfino, assistente nell' Istituto di clinica medica della R. Università di Genova. Paper. Price, 15 lire. Pp. 135, with illustrations. Rome: Luigi Pozzi, 1935.

This Italian monograph on the pineal body will be of interest to American readers chiefly by reason of its extensive bibliography, which includes over 300 references. The literature is covered to 1934; more recent publications of Engel, Saphir, Rowntree and his collaborators and other workers on the physiologic effects of pineal extracts are therefore not considered. The author presents brief summaries of knowledge of the pineal gland from many aspects, historical, phylogenetic, anatomic, histologic and physiologic, the latter including what little is known of its endocrine function and its functional relation to other organs.

Methodik der medizinischen Erbforschung unter besonderer Berücksichtigung der Psychiatrie. Von Dr. Bruno Schulz, Assistent am Kaiser Wilhelm-Institut für Genealogie und Demographie der Deutschen Forschungsanstalt für Psychiatrie in München. Paper. Price, 10.50 marks. Pp. 189, with 16 illustrations. Leipzig: Georg Thieme, 1936.

This is an extremely technical work concerning methods of handling statistical data on heredity. There are numerous mathematical equations, which a clinician will have difficulty grasping. The conclusions regarding the rôle of heredity in the production of psychoses are dealt with elsewhere. The book represents the technical attitude of the workers in the Munich institute toward the general problem. Once the material is obtained, it is probably satisfactorily handled mathematically. The clinican, however, wonders about the accuracy of diagnosis, the type of clinical records and the longitudinal studies of individual patients as they may affect the stuff with which the statistician deals.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Health Insurance: Disability Due to Myocarditis Resulting from Pneumonia.—The defendant insurance company agreed to pay certain benefits to the plaintiff if he became disabled. Liability was limited to a maximum period of six weeks if he became disabled because of "any chronic or recurring disease." The plaintiff had pneumonia, which resulted in myocarditis from which disability ensued. The insurance company refused to pay more than the limited benefits provided in the policy. The plaintiff therefore sued and obtained judgment, from which the company appealed to the Supreme Court of Appeals of West Virginia.

The insurance company contended that since the plaintiff's disability was caused by a "chronic or recurring disease," myocarditis, he was entitled only to the limited benefits. The plaintiff protested that even though myocarditis is a "chronic or recurring disease" his disability actually grew out of his original illness, pneumonia, and that he was entitled to the full benefits provided by the policy. If, said the Supreme Court of Appeals, the meaning of the language of an insurance policy is in doubt, it should be construed favorably to the insured. In the present case, the insurance company assumed the risk of illness from pneumonia and also the risk of all the direct results of that disease. The circumstance that pneumonia directly resulted in a condition that could be described as another and different disease makes no difference. As long as it is a condition definitely attributed to the occurrence of the risk insured against, the fact that its severity may justify classifying it as an independent disease is not a determining factor. The insured undoubtedly had pneumonia and the pneumonia undoubtedly caused the heart condition that compelled him to give up his work. The plaintiff was therefore entitled to the maximum benefits provided by the policy. Judgment in favor of the plaintiff was affirmed.—*White v. Inter-Ocean Casualty Co. (W. Va.), 185 S. E. 203.*

Accident Insurance: "Death Resulting from Accidental Suffocation by Gases" Construed.—The defendant insurance company issued to the insured two accident insurance policies in which it promised to pay certain benefits in case the insured died but limited liability to $600 in event of "death resulting from accidental suffocation by illuminating or other gases or the accidental taking of any poison." Three days after the policies were issued, the insured was found in his garage overcome by the fumes escaping from the motor of his automobile. He died a few minutes later from carbon monoxide poisoning. The defendant claimed that the death resulted "from accidental suffocation by illuminating or other gases" and that therefore it was liable only to the extent of $600. The plaintiff, the beneficiary under the policies, brought suit to recover the maximum benefits. The trial court sustained the defendant's motion to withdraw from the jury the question of liability over and above $600 and, with the consent of the defendant, entered a judgment for the plaintiff for that amount. The plaintiff thereupon appealed to the Supreme Court of Nebraska.

It was not disputed, said the court, that the insured died as a result of his inhaling the fumes from the exhaust of his automobile. That the death was therefore caused by the inhalation of gas cannot be denied. In *Birss* v. *Order of United Commercial Travelers,* 109 Neb. 226, 190 N. W. 486, it was said:

> The term "gas" is, in a sense, a generic term and is broad and sweeping in its meaning. In Webster's Unabridged Dictionary it is defined as "an aeriform fluid; a term used at first by chemists as synonymous with air, but since restricted to fluids supposed to be permanently elastic, as oxygen, hydrogen, etc., in distinction from vapors, as steam, which become liquid on a reduction of temperature. In present usage, since all of the supposed permanent gases have been liquefied by cold and pressure, the term has resumed nearly its original signification, and is applied to any substance in the elastic or aeriform state."

The contention of the beneficiary was that death had not resulted from accidental *suffocation,* relying apparently on medical testimony to the effect that inhaled carbon monoxide gas does not stay in the lungs and does not therefore act as a mechanical barrier to respiration. Death results when there is sufficient concentration of carbon monoxide combined with the hemoglobin or red blood cells to displace the oxygen. But, said the court, in construing the contract of insurance, words used therein will be considered as used in their ordinary and popular sense. The definitions or constructions placed on them by the scientist or expert cannot control. "Suffocate," continued the court, is defined in Webster's New International Dictionary as "to kill by stopping respiration, as by strangling or asphyxiation," while the same authority defines "asphyxiation" as "a state of asphyxia; suffocation," and "asphyxia" as "apparent death, or suspended animation, in living organisms, due to deficiency of oxygen and excess of carbon dioxide, specif., in the blood, as in interruption of respiration from suffocation or drowning, or from the inhalation of irrespirable gases." "Suffocation" is defined in Dorland's American Illustrated Medical Dictionary (ed. 16) as "the stoppage of respiration, or the asphyxia that results from it," while the same authority defines "asphyxia" as "suffocation; also suspended animation from suffocation or a deficiency of oxygen in the blood."

In view of these definitions, the court was convinced that a person suffers death as the result of suffocation by gas whether death was due to a deficiency of oxygen in the blood or to an interruption of the physical act of breathing that would prevent the inhalation of sufficient oxygen into the lungs. The judgment of the trial court for the plaintiff for the limited benefits provided in the policies was therefore affirmed.—*Stone v. Physicians Casualty Assn. of America (Neb.), 266 N. W. 605.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Cleveland, Jan. 11-13. Dr. Philip Lewin, 55 East Washington St., Chicago, Secretary.

American Orthopsychiatric Association, New York, Feb. 18-20. Dr. George S. Stevenson, 50 West 50th St., New York, Secretary.

Annual Congress on Medical Education, Medical Licensure and Hospitals, Chicago, Feb. 15-16. Dr. William D. Cutter, 535 North Dearborn St., Chicago, Secretary.

Eastern Section, American Laryngological, Rhinological and Otological Society, Boston, Jan. 7. Dr. D. C. Jarvis, Quarry Bank Bldg., Barre, Vt., Chairman.

Middle Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 11. Dr. Alfred Lewy, 25 East Washington St., Chicago, Chairman.

Mid-Western Section, American Laryngological, Rhinological and Otological Society, Chicago, Jan. 11. Dr. Frederick A. Figi, 436 Tenth Ave. S.W., Rochester, Minn., Chairman.

Pacific Coast Surgical Association, Seattle, Wash., and Victoria, B. C., Feb. 24-27. Dr. H. Glenn Bell, University of California Hospital, San Francisco, Secretary.

Society of Surgeons of New Jersey, Newark, Jan. 6. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Memphis, Tenn., Jan. 13. Dr. Charles D. Blassingame, Physicians and Surgeons Bldg., Memphis, Tenn., Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, San Diego, Calif., Jan. 30-31. Dr. David R. Higbee, 3245 Fourth Ave., San Diego, Calif., Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1926 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them. Titles marked with an asterisk (*) are abstracted below.

American Journal of Cancer, New York

28: 233-460 (Oct.) 1936

*Virus Tumors and Tumor Problem. P. Rous, New York.—p. 233.
Solid Teratoid Tumors of Anterior Mediastinum: Report of Two Cases. J. P. Fox and C. A. Hospers, Chicago.—p. 273.
Ovarian Tumor of Brenner Type. F. Proescher and J. Rosasco, San Jose, Calif.—p. 291.
Significance of Amino Acids for Growth in Vitro of Human Fibroblasts: I. Growth Inhibiting Action of Glycine. J. P. M. Vogelaar and Eleanor Erlichman, New York.—p. 301.
Effects of Osmotic Pressure on Normal and Malignant Fibroblasts. A. M. Brues and Claire McTiernan Masters, Boston.—p. 314.
Permeability of Normal and Malignant Cells to Water. A. M. Brues and Claire McTiernan Masters, Boston.—p. 324.
Studies in Carcinogenesis: III. Isomers of Cholanthrene and Methylcholanthrene. M. J. Shear, Boston.—p. 334.
Further Quantitative Methods for Study of Transplantable Tumors: Growth of R39 Sarcoma and Brown-Pearce Carcinoma. R. Schrek, Nashville, Tenn.—p. 345.
Effect of Size of Inoculum on Growth of Transplantable Rat Tumors. R. Schrek, Nashville, Tenn.—p. 364.
Permanent and Transient (Fortuitous) Variations of Growth Components of Transplantable Rat Ttumors. R. Schrek, Nashville, Tenn.—p. 372.
Method for Counting Viable Cells in Normal and in Malignant Cell Suspensions. R. Schrek, Nashville, Tenn.—p. 389.
Carcinoma of Breast in Homologous Twins. S. A. Munford and H. Linder, Clifton Springs, N. Y.—p. 393.

Virus Tumors.—Rous deals with the difficulties that stand in the way of the supposition that the general run of malignant growths are due to viruses. 1. The cause of cancer must be present wherever man is. But wherever he goes so do certain of his parasites. May he not take viruses as well? 2. The sporadic occurrence of cancers attests the lack of infectiousness. The natural incidence of the chicken tumors yields no sign whatever that they are caused by a virus. Their occurrence is highly conditioned and some of them obviously represent a triumph over resistance offered by the host. 3. In the failure of attempts to demonstrate an extrinsic cause for the generality of malignant mammalian tumors, technical difficulties may have been mistaken for a biologic principle. 4. The appearance of malignant tumors of the same sort in identical twins or in hereditary glioma of the retina and in von Recklinghausen's disease may mean no more than that when the soil and the contributory circumstances are right a carcinogenic agent, perhaps a virus, is effective as it would not otherwise be. 5. The experimental induction of cancer at sites where it never occurs normally indicates that some decisive condition or agent is evidently present in the areas at which they arise. Andrewes has given reasons for supposing this agent to be a virus entering the organism previously and ensconced in the epithelium at the time when the carcinogenic substance is applied—an indigenous virus, as he terms it. 6. Cancer does not spring full blown from normal cells but develops as the result of gradual and often long continued changes: The changes induced by all the various carcinogenic agents may be of a sort to urge a symbiotic virus or viruses to pathogenic activity. 7. Metastases of several differing sorts, representative of more than one germ layer, are occasionally encountered in patients dying of a teratoma that becomes malignant. Many teratomas are supposedly derived from pluripotential sex cells and, if one of these became infected with a tumor-producing virus, secondary growths of diverse character would occur as a matter of course. 8. Since viruses are highly specific in their action, one causing osteochondrosarcomas of the fowl, for example, another endotheliomas only, an entire microcosm of viruses would be needed to account for all the malignant tumors. The assumption that certain tumors may be due to viruses should be accepted only so far as to lead one to make tests with these growths.

American Journal of Medical Sciences, Philadelphia

192: 589-744 (Nov.) 1936

Protamine Insulin in Treatment of Diabetes Mellitus. W. R. Campbell, A. A. Fletcher and R. B. Kerr, Toronto.—p. 589.
Incidence and Differential Diagnosis of Hypoglycemic Convulsions. E. Ziskind, B. S. Hollombe and Ruth O. Bolton, Los Angeles.—p. 600.
Supplemental Report of Case of Essential Pentosuria of Twenty-Eight Years' Standing, with Study of Specific Pentose Present. S. Solis-Cohen and L. Gershenfeld, Philadelphia.—p. 610.
Phenolemia and Indoxylemia: Their Origin, Significance and Regulation. B. A. Houssay, Buenos Aires, Argentina, South America.—p. 615.
*Clinical Observations at High Altitude: Observations on Six Healthy Persons Living at 17,500 Feet and Report of One Case of Chronic Mountain Sickness. J. H. Talbott and D. B. Dill, Boston.—p. 626.
Thevetin in Thyrotoxicosis. T. B. Noble Jr. and K. K. Chen, Indianapolis.—p. 639.
Use of Evipal (N-Methylcyclohexenylmethyl Barbituric Acid) in Coronary Occlusion: Note. S. Hirsch, New York.—p. 644.
Atabrine Pigmentation. A. J. Schechter and H. M. Taylor, Durham, N. C.—p. 645.
Localized Radiculitis and Neuritis: Their Diagnosis and Treatment. J. C. Yaskin and C. A. Patten, Philadelphia.—p. 650.
*Is There Any Relationship Between Resistance and Susceptibility to Poliomyelitis and Diphtheria? C. W. Jungeblut, New York.—p. 661.
Relation of Physical Defects to Nutritional Impairment, Based on Examination of 30,000 Children of Twenty-One States: Physical Measurement Studies Number Five. W. M. Gafafer, Washington, D. C.—p. 669.
Riedel's Struma. D. Eisen, Toronto.—p. 673.
Eosinophilia and Skin Tests in Diagnosis of Trichinosis. R. A. Kilduffe, Atlantic City, N. J.—p. 689.
Cystometric Studies: Value of Follow-Up Examinations. M. Muschat, Philadelphia.—p. 693.
Higher Carbohydrate Diets in Treatment of Diabetes. F. B. Peck, Indianapolis.—p. 697.
Glucose Tolerance in Paget's Disease (Osteitis Deformans): Note. F. L. Apperly and M. Katharine Cary, Richmond, Va.—p. 702.
Agranulocytosis Following Ingestion of Cinchophen: Case. S. Shapiro and L. Lehman, New York.—p. 705.

Clinical Observations at High Altitude.—Talbott and Dill consider that the residence of from two to fourteen years of six healthy workmen at 17,500 feet is sufficient to call them permanent inhabitants. The unanimous admission of symptoms of acute mountain sickness in the first days after arrival at this altitude suggests that their occurrence is no indication of the ability to become acclimated to elevations as high as 17,500 feet. Colloid goiter and hyperthyroidism were not observed in any of the workmen. Other significant points in the physical examinations were normal blood pressure, a normal respiratory rate at rest, an emphysematous-like contour to the chest and clubbing of the fingers. In three subjects the pulmonic second sound was accentuated and greater than the aortic second sound. The average pulse rate for the six men at rest was 64. The absence of tachycardia at a high altitude suggests that the tachycardia of cardiac decompensation is not directly related to anoxemia. The data obtained from the examination of the arterial blood show among other changes a large increase in the oxygen capacity, cell volume and red cell count. The lowest saturation of arterial blood observed was 67.6 per cent, the highest was 84.6 per cent and the average for the six men was 75 per cent. In ten temporary residents at the same time of year at this altitude the average saturation was 76.2 per cent. The absence of any difference between the arterial saturation in the temporary and the permanent residents suggests that permanent acclimation is not associated with any significant change in this function of the blood. The average concentration of hemoglobin in cells for normal men at sea level is from 44 to 46 per cent of their volume of cells per liter. The average for the six subjects was 44. The carbon dioxide content of arterial serum varied between 30 and 40 per cent of its volume for the six men. The p_H of the arterial serum reflected a mild degree of acidosis. The serum concentrations of potassium and chloride were normal or above normal and the concentrations of sodium were below normal. The concentrations of protein and calcium were within normal limits. The environment, symptomatology, physical examination and laboratory data of mountain sickness are distinct and in their totality are unlike any other disease. The syndrome represents more than the physiologic response to a high altitude. The disease is associated with prolonged anoxemia but the part that this plays in the pathogenesis is uncertain. Chronic mountain sickness is a progressive disease which manifests a remarkable recovery under increased oxygen pressure.

Resistance and Susceptibility to Poliomyelitis and Diphtheria.—In a series of neutralization tests with sixteen diphtheria antitoxic horse serums, Jungeblut secured complete inactivation of poliomyelitis virus of four samples and partial inactivation of one sample. There was no relationship between antitoxic potency and poliocidal power. Three monkeys that survived a full course of active immunization against diphtheria were protected against intracerebral infection with poliomyelitis virus. On reinfection, two animals developed a slight paresis, the third remaining entirely free from any symptoms of the disease. Poliocidal substances, although occasionally demonstrable in the serum of diphtheria-immune monkeys, appear with marked irregularity and show no correlation to the degree of antitoxic immunity, and their concentration at best is only very weak. The author sent 350 questionnaires in an attempt to gather further data as regards the relative frequency of diphtheria and poliomyelitis in the same child. Only 182 replies were received, with partial or complete answers. Among these were sixteen cases giving a definite history of diphtheria before the attack of poliomyelitis. This would tend to indicate a greatly increased incidence of diphtheria among the group of poliomyelitis patients (ages mostly from 1 to 10 years) when contrasted with the attack rate of diphtheria for the child population at large in New York City in the standard age group of from 1 to 9 years during the same period, which varied from 1.97 to 1.2 per thousand. Precise data as to the absence or presence of previous antidiphtheritic immunization and the clinical type of the disease were obtained from 165 returns. Among a group of seventy cases of poliomyelitis developing in children previously immunized against diphtheria, forty-five were of the paralytic type and twenty-five were listed as abortive. The other group of ninety-five cases of poliomyelitis developing in children who gave no history of previous antidiphtheritic immunization included seventy-five paralytic and twenty abortive cases. The material is meager, but it would seem that the incidence of paralysis was somewhat reduced in the diphtheria-immune children. The data are strongly suggestive of the operation of some common basic mechanism that governs susceptibility and resistance to both poliomyelitis and diphtheria.

American Journal of Physiology, Baltimore

117: 189-380 (Oct.) 1936. Partial Index

Skin Potential and Impedance Responses with Recurring Shock Stimulation. T. W. Forbes, New York.—p. 189.
Glomerular Filtration and Urea Excretion in Relation to Urine Flow in Dog. J. A. Shannon, New York.—p. 206.
*Effect of Acute Hemorrhage on Emptying Time of Stomach. E. J. Van Liere, C. K. Sleeth and D. Northup, Morgantown, W. Va.—p. 226.
Total Plasmapheresis. J. B. Stanbury, Edna Warweg and W. R. Amberson, with technical assistance of Verda I. McLendon.—p. 230.
Activity of Cardiac Sympathetic Centers. D. W. Bronk, L. K. Ferguson, R. Margaria and D. Y. Solandt, Philadelphia.—p. 237.
Study of Speed of Absorption Following Ingestion of Glucose and of Sucrose. Alice C. Roberts, Chicago.—p. 257.
Spinal Path for Responses to Cerebellar Stimulation. E. H. Ingersoll, H. W. Magoun and S. W. Ranson, Chicago.—p. 267.
Blood Flow in Circumflex Branch of Left Coronary Artery of Intact Dog. H. E. Essex, J. F. Herrick, E. J. Baldes and F. C. Mann, Rochester, Minn.—p. 271.
Carotene and Associated Pigments in Medullated Nerve. J. P. Bartz and F. O. Schmitt, St. Louis.—p. 280.
Absorption of Sodium Chloride from Small Intestine at Various Degrees of Anoxemia. E. J. Van Liere and C. K. Sleeth, Morgantown, W. Va.—p. 309.
Increased Water Exchange Following Eck Fistula in Dogs. L. A. Crandall Jr. and G. M. Roberts, Chicago.—p. 318.
Glucose Utilization of Phlorhizinized Dogs After Hepatectomy. D. R. Drury, H. C. Bergman and P. O. Greeley, Los Angeles.—p. 323.
Distribution of Glucose in Blood. I. Neuwirth, New York.—p. 335.
Comparison of Electrogram of Optic Cortex with That of Retina. S. H. Bartley, St. Louis.—p. 338.
Respiratory Reactions on Vertical Movements. E. A. Spiegel, Philadelphia.—p. 349.
Temporal Summation in Peripheral Nerve Fibers. E. A. Blair and J. Erlanger, St. Louis.—p. 355.

Effect of Hemorrhage on Emptying Time of Stomach.—Van Liere and his associates determined the normal gastric emptying time fluoroscopically in four healthy male subjects. After one tenth of their calculated blood volume was withdrawn, the gastric emptying time was prolonged an average of 41 per cent. In no case was it less than 25 per cent. Twenty-four hours after the hemorrhage, three of the four men still showed a delay of from 15 to 20 per cent. One subject showed no delay twenty-four hours after the blood had been withdrawn. At the end of forty-eight hours the stomach had apparently regained its normal motility in all the subjects. The observations were also made on two dogs. They too showed a distinct prolongation in gastric emptying time.

Archives of Neurology and Psychiatry, Chicago

36: 917-1154 (Nov.) 1936

Prognosis of Lethargic Encephalitis in Childhood. W. Healy, Boston.—p. 921.
Cerebrospinal Fluid Pressure. L. J. Pollock and B. Boshes, Chicago.—p. 931.
Radiculoneuritis with Acellular Hyperalbuminosis of Cerebrospinal Fluid. G. Guillain, Paris, France.—p. 975.
Aggressive-Submissive Behavior and Fröhlich Syndrome. D. M. Levy, New York.—p. 991.
Amphithymia: Some Syndromes of Depression and Elation. N. L. Blitzsten, Chicago.—p. 1021.
*Constitutional Differences Between Deteriorated and Nondeteriorated Patients with Epilepsy: I. Stigmas of Degeneracy. H. A. Paskind and M. Brown, Chicago.—p. 1037.
Frequency of Epilepsy in Offspring of Persons with Epilepsy, with Especial Reference to Differences Between Institutional and Extramural Patients. H. A. Paskind and M. Brown, Chicago.—p. 1045.
Emotional Factors in Mental Retardation: Reading Problem. R. C. Hamill, Chicago.—p. 1049.
*Klippel-Feil Syndrome: Pathologic Report. L. W. Avery and C. C. Rentfro, Chicago.—p. 1068.
Regeneration of Posterior Root Fibers in the Cat. H. A. Paskind, Chicago.—p. 1077.
Meningo-Encephalomyelitis Neonatorum: Anatomic Report of Case. R. Richter, Chicago.—p. 1085.

Epilepsy.—Paskind and Brown discuss the differences in the presence of stigmas of degeneracy (malformations about the head and face) in epileptic patients with and without deterioration. They believe that stigmas of degeneracy may be accepted as constitutional, since they are developmental anomalies which remain unchanged throughout life, except for changes implicit in growth. The material for the comparisons consisted of seventy-nine epileptic patients with deterioration from three state hospitals and thirty-nine patients with no deterioration from three outpatient clinics. In order to allow time for deterioration to occur, no patient was accepted for the group of those not showing deterioration unless he had had seizures for at least four years; many of these patients had had seizures for decades. The results of the investigation show that all stigmas, with the exception of attachment of the ear lobe, accessory anthelix, partially fused helix and anthelix, unusually prominent upper lip and abnormally high palate, were more common in the deteriorated patients. In most instances these differences were marked, certain stigmas occurring several times as frequently in the deteriorated as in the nondeteriorated patients. In other instances certain anomalies were found in the deteriorated patients that were absent in the nondeteriorated patients. Anomalies of the eye were more than twice as common in deteriorated than in nondeteriorated patients, and those of the teeth were more than three times as common. Anomalies of the skull were less than one-third as frequent in nondeteriorated patients; those of the nose were one-half as frequent. Defects in palatal structure were almost twice as common in deteriorated as in nondeteriorated subjects. Of the deteriorated patients 56.6 per cent had twelve or more stigmas; in the group of nondeteriorated patients such profuse stigmatization did not occur in a single instance. It seems reasonable to believe that there is a correlation between stigmas of degeneracy (somatic developmental anomalies) and cerebral developmental anomalies. This suggests that an essential difference between institutionalized deteriorated and extramural nondeteriorated patients with epilepsy may be the more frequent presence of cerebral developmental anomalies in the patients with deterioration.

Klippel-Feil Syndrome.—Avery and Rentfro report a case of the Klippel-Feil syndrome with a pathologic study of the changes in the spinal cord. Not only did abnormalities exist in the upper portion of the dorsal and in the cervical region but throughout the dorsal vertebrae there was a cleft appearance of the bodies, seemingly indicating that the two developing halves of the body did not fuse well in the midline. What might be a hemivertebral body was seen in the instance of the second dorsal vertebra. There was also evidence that fusions occurred between the vertebral bodies. The segments of the

vertebral column were fairly well represented by the number of vertebral arches. It is suggestive that there was numerical reduction not of the segments but only of the vertebral bodies. The character of the defect in the spinal cord was also in the nature of a cleft in the posterior aspect of the cervical and the upper portion of the dorsal region. At these levels complete formation of the spinal cord failed to occur, so that a central canal was not formed but was represented by a layer of ependymal cells lining the posterior margins of the cord. Even at lower levels, at which the cord had been formed completely, the central canal was of abnormal location, size and contour. Other structures also were involved in the defect, as evidenced by gliosis of the posterior columns and distinct deviations in the character of the blood vessels and the connective tissue. These changes are referable to defects occurring in the formation of the original neural tube and are, the authors believe, a true expression of dysraphia.

Archives of Surgery, Chicago

33: 733-912 (Nov.) 1936

Neurofibroma and Neurofibrosarcoma of Peripheral Nerves Unassociated with Recklinghausen's Disease: Report of Twenty-Five Cases. E. C. Cutler and R. E. Gross, Boston.—p. 733.
Effect of Posterior Pituitary Extracts on Motility of Gastro-Intestinal Tract. H. Necheles, M. Maskin, S. Strauss, A. A. Strauss and E. Taft, Chicago.—p. 780.
Leiomyoma of Stomach. J. H. Conway, New York.—p. 792.
Hypoparathyroidism Following Operation for Hyperparathyroidism Due to Adenoma Tolerance for Parathyroid Extract. R. D. McClure, Detroit.—p. 808.
Spinal Anesthesia: Experimental Basis of Some Prevailing Clinical Practices. Co-Tui, New York.—p. 825.
*Congenital Abnormal Arteriovenous Anastomoses of Extremities, with Especial Reference to Diagnosis by Arteriography and by Oxygen Saturation Test. J. R. Veal and W. M. McCord, New Orleans.—p. 848.
Cranial Venous Sinuses: Correlation Between Skull Markings and Roentgenograms of Occipital Bone. B. Woodhall and A. E. Seeds, Baltimore.—p. 867.
Preparation of Operative Field: Report of Survey of Seventeen Surgical Teaching Clinics. W. C. Beck, Chicago.—p. 876.
Lesions of Thyroglossal Tract. J. C. McClintock, Albany, N. Y.—p. 890.
Sixty-First Report of Progress in Orthopedic Surgery. J. G. Kuhns, E. F. Cave, S. M. Roberts, J. S. Barr and R. J. Joplin, Boston; J. A. Freiberg, Cincinnati; J. E. Milgram, New York, and R. I. Stirling, Edinburgh, Scotland.—p. 895.

Congenital Arteriovenous Anastomoses of Extremities.—Veal and McCord present seven cases of congenital abnormal arteriovenous anastomoses of the extremities. The underlying principle, as stated by Sabin and by Woollard, is that the common capillary plexus on which both arteries and veins develop is the basis for the persistence of a direct communication between the two systems. That the condition is not often considered a diagnostic possibility is shown by the fact that, of the twenty-three cases reported by Horton from the Mayo Clinic, in only one was the condition recognized prior to the patient's admission. Undoubtedly many cases have been overlooked in all clinics, while in others the disease has been diagnosed as varicose veins or ulcers, trophic ulcers, thrombophlebitis, arthritis, elephantiasis or peripheral vascular disease and treated accordingly. The first principle of diagnosis is a careful history. All patients should be questioned closely concerning the onset of their varicosities, the location of the first noted and the possible etiologic factors involved. Cases of varicose veins which follow thrombophlebitis, infections of various sorts, surgical incisions and repeated pregnancies rarely need further consideration from this standpoint. But the group of cases in which the varicosities present early in life, without obvious cause, in which they are unilateral and in unusual locations and in which they are associated with ulceration, arthritic changes and hemihypertrophy need further consideration, though again only a small number of them will prove to be true abnormal arteriovenous communications. The cases should be studied by gross comparative examination of specimens of blood from the normal and from the affected extremity, by the oxygen saturation test and by arteriography. The oxygen saturation test reveals the exact location of the anastomosis and is of decided value in cases in which the anastomosis is not sufficiently extensive to change the character of the blood throughout the limb and in which the diagnosis may be missed because the specimen of blood is taken from an area too remote from it to be affected by it. By means of arteriography it is now possible to locate the supposed anastomosis with absolute accuracy as well as merely to confirm its existence. Injection of the vascular system with stabilized solution of colloidal thorium dioxide demonstrates as no other method can the exact site of the abnormal communication, its size and the number and extent of the vessels involved. The arteriograms are not always easy to interpret, and abnormalities involving the small arteries and veins can be detected then only by comparison with normal standards. Through use of arteriography it is possible to determine which patients should be treated by surgical measures, which can safely be treated by the injection of sclerosing substances if the Perthes test demonstrates the adequacy of the deep circulation and which must be left untreated unless and until amputation proves necessary.

Journal Industrial Hygiene and Toxicology, Baltimore

18: 471-582 (Oct.) 1936

Effects of Heat and Humidity on Human Body. C. K. Drinker, Boston.—p. 471.
Physiologic Effects of High Pressures. L. A. Shaw, Boston.—p. 486.
Industrial Operations in Compressed Air. O. Singstad, New York.—p. 497.
Causation of Pneumoconiosis. P. Drinker, Boston.—p. 524.
Clinical Aspects, Diagnosis and Treatment of Pneumoconiosis. W. I. Clark, Boston.—p. 537.
Incidence of Silicosis in Trap Rock Quarry Workers as Determined by X-Ray. L. J. Goldwater, New York.—p. 550.
Chronic Nicotine Toxicity: I. Feeding of Nicotine Sulfate, Tannate and Bentonite. R. H. Wilson and F. DeEds, San Francisco.—p. 553.
Id.: Effect of Nicotine-Containing Diets on Blood Sugar Concentration of Albino Rat. R. H. Wilson and F. DeEds, San Francisco.—p. 565.
Toxic Encephalopathy and Volatile Solvents in Industry: Report of Case. Dorothy E. Donley, Cincinnati.—p. 571.

Journal of Lab. and Clinical Medicine, St. Louis

22: 113-220 (Nov.) 1936

Bacteriologic Studies of Blood of Normal Individuals and Rheumatic Fever Patients. Esther Meyer and Virginia Ryan, Chicago.—p. 113.
Xylose Tolerance of Rabbits with Uranium Nephritis. H. W. Larson, New York.—p. 117.
Agranulocytosis in the Negro: Case Report with Etiology and Comment. J. C. Norris, Atlanta, Ga.—p. 125.
Rate of Disintegration of Platelets. I. Olef, Boston.—p. 128.
*Value of Air Conditioned Rooms in Treatment of Seasonal and Perennial Asthma. A. Trasoff and G. Blumstein, Philadelphia.—p. 147.
Primary Carcinoma of Thymus Gland: Case Report. H. A. Slesinger, Windber, Pa.—p. 151.
*Fever Accompanying Induced Reticulocyte Crisis of Pernicious Anemia. W. M. Fowler, Iowa City.—p. 155.
Blood Picture in Two Cases of Agranulocytosis: Following Treatment with Neoarsphenamine, with Especial Reference to Myelocytes and Juveniles. J. P. Crawford, Washington, D. C.—p. 157.
Studies on Circulation: Dye Injection Method: Effect of Digitalis on Patients with Normal Cardiovascular Systems. J. W. Moore and J. M. Kinsman, Louisville, Ky.—p. 165.
Relationship of Vitamin C to Hemorrhagic Diatheses. D. J. Stephens and Estelle E. Hawley, Rochester, N. Y.—p. 173.
Study of Decamethylenediguanidine Bitartrate (Anticoman). P. L. Ewing and H. Segenreich, Chicago.—p. 180.

Air Conditioned Rooms in Treatment of Asthma.—The results of Trasoff and Blumstein with forty asthmatic patients confirm those of Gay, who was able to obtain favorable results in his asthmatic patients within one hour after their admission to an air conditioned room, and that of Nelson, Rappoport and Walker, who report 50 per cent improvement in their asthmatic patients within three hours or less. Only certain extrinsic forms of asthma are likely to benefit from this method of treatment. One should not expect to obtain relief in such an atmosphere when sensitivity exists to the animal danders, which are contained in that room, such as feathers. Intrinsic factors are not controlled or removed. As in the case of Gay, patients suffering from bacterial allergy cannot expect any benefit in such rooms. This explains the failure of treatment in the perennial as well as mixed asthmatic patients in air conditioned atmospheres. The air conditioned room has some diagnostic value. Failure to obtain immediate relief in such an atmosphere would justify the exclusion of pollen as a factor.

Fever Accompanying Pernicious Anemia.—In a series of 206 cases of pernicious anemia in which remissions were induced by liver therapy, Fowler observed fever ranging from 102.4 to 106 F. coincident with the reticulocyte crisis in eight

cases. In each of these cases a concentrated form of liver extract was administered, to one patient intramuscularly, to the others orally. Every conceivable extraneous cause for fever was excluded. The temperature rose rather suddenly, returning to normal more gradually over a period of from twenty-four to forty-eight hours. In two cases in which reticulocyte counts were being done daily, the highest temperature coincided exactly with the highest reticulocyte count and in three it occurred during the period of decline. In the three cases in which reticulocyte counts were not made, the fever appeared during the time when the crisis was to be expected. In several of the cases the fever was accompanied by a slight chill; in the others there were no associated symptoms of any kind. None of the patients had a leukocytosis. There was no apparent relationship between the occurrence of fever and the pretherapeutic erythrocyte level. The continuous low grade fever characteristic of pernicious anemia during relapse, manifested by many of the 206 patients, disappeared in most cases after the reticulocyte crisis. The fever observed was not referable to the reticulocytosis alone, and the authors are unable to give a satisfactory explanation of its mechanism.

Journal of Nutrition, Philadelphia

12: 329-428 (Oct. 10) 1936

Factors Influencing Incidence of Dietary Hemorrhagic Disease in Chicks. H. J. Almquist and E. L. R. Stokstad, Berkeley, Calif.—p. 329.

Metabolic Studies of Eskimos in the Canadian Eastern Arctic. I. M. Rabinowitch and Florence C. Smith, with technical assistance of Eleanor V. Bazin and Marjorie Mountford, Montreal.—p. 337.

Influence of Vitamins A, B or D, Anemia or Fasting on Rate of Fat Absorption in Rat. Margaret House Irwin, H. Steenbock and A. R. Kemmerer, with technical assistance of Janet Weber, Madison, Wis.—p. 357.

Influence of Certain Hydrotropic and Other Substances on Fat Absorption. Margaret House Irwin, Janet Weber and H. Steenbock, Madison, Wis.—p. 365.

Relation of Calcium and of Iron to Erythrocyte and Hemoglobin Content of Blood of Rats Consuming a Mineral Deficient Ration. J. M. Orten, A. H. Smith and L. B. Mendel, New Haven, Conn.—p. 373.

Inverse Relation Between Growth and Incidence of Cataract in Rats Given Graded Amounts of Vitamin G-Containing Foods. P. L. Day and W. J. Darby, Little Rock, Ark.—p. 387.

Blood Sugar in Rats Rendered Cataractous by Dietary Procedures. P. L. Day, Little Rock, Ark.—p. 395.

Comparison of Biologic and Chemical Methods for Determination of Vitamin C in Canned Strained Vegetables and Study of Its Variation from Year to Year. Flora Hanning, East Lansing, Mich.—p. 405.

*Storage of Vitamin C by Normal Adults Following a Period of Low Intake. Patricia H. O'Hara and Hazel M. Hauck, Ithaca, N. Y.—p. 413.

Storage of Vitamin C by Normal Adults.—O'Hara and Hauck planned and administered to four normal women a basal diet adequate in other respects but containing only 5 mg. of vitamin C. They found that the amount of vitamin C necessary to restore the tissues to saturation after a month on this diet ranged from 2,200 to 2,800 mg. when administered in daily doses of 200 mg. The difference between intake and excretion up to the point of saturation following prolonged deprivation of vitamin C may afford some indication of the maximal vitamin C reserve. On this basis, tissue reserves at saturation appear to be of the order of from 2,500 to 3,000 mg. In these experiments, capillary resistance did not give an adequate indication of the state of nutrition with respect to vitamin C.

New Orleans Medical and Surgical Journal

89: 211-266 (Nov.) 1936

Endemic Typhus. W. H. Seemann, New Orleans.—p. 211.

Some Public Health Aspects of Parasitic Infections in the Southern United States, with Especial Reference to Louisiana. E. C. Faust, New Orleans.—p. 213.

Physical Defects of Children of Preschool and School Age. E. A. Socola, New Orleans.—p. 221.

Congenital Heart Disease with Presentation of Case and Pathologic Specimens. Rena Crawford, New Orleans.—p. 223.

Some Principles in Treatment of Fractures of Forearm. H. T. Simon, New Orleans.—p. 227.

Management of Ruptures of Posterior Urethra: Remarks Concerning Alkaline Urinary Infections. M. H. Foster, Alexandria, La.—p. 232.

Empyema Thoracis. M. T. Green, Ruston, La.—p. 237.

Reactions of Relatives: Problem in Psychiatry. L. L. Cazenavette, New Orleans.—p. 240.

Simple and Efficient Aid in Diagnosis of Endocrine Dysfunctions. R. A. Paine, Shreveport, La.—p. 244.

Oklahoma State Medical Assn. Journal, McAlester

29: 383-424 (Nov.) 1936

Cough: Its Relation to Pharyngeal and Nasal Infection. L. C. McHenry, Oklahoma City.—p. 383.

Acute Otitis Media in Children. H. C. Childs, Tulsa.—p. 387.

Treatment of Pneumonia. R. Q. Goodwin, Oklahoma City.—p. 388.

Recent Outbreak of Lobar Pneumonia in Tulsa and Vicinity. S. Goodman, Tulsa.—p. 392.

Empyema. J. B. Gilbert, Tulsa.—p. 397.

Use of Papain in Prevention of Reformation of Peritoneal Adhesions. B. W. Ward, Tulsa.—p. 399.

Therapeutic Uses of Medicinal Gases in Office and Bedside Practice. Mary Edna Sippel, Tulsa.—p. 402.

Rhode Island Medical Journal, Providence

19: 151-170 (Oct.) 1936

*Narcosis Therapy in Psychoses. G. H. Alexander, Providence.—p. 151.

History of the Rhode Island Hospital. J. M. Peters, Providence.—p. 155.

19: 171-186 (Nov.) 1936

The Schilling Hemogram in Appendicitis. H. E. Gauthier, Woonsocket.—p. 173.

Coronary Thrombosis. R. I. Lee, Boston.—p. 177.

Narcosis Therapy in Psychoses.—During the last six months Alexander employed deep narcosis therapy in five cases, in one of which discontinuance of the therapy was forced on the fourth day, because of potentially dangerous physical complications. Of the four completed cases, two patients were well enough to leave the hospital approximately one week following narcosis therapy and have remained entirely well for periods of four and six months respectively. Both of these patients presented variable degrees of excitement, bizarre behavior, delusions and probably hallucinosis and were classified as schizophrenic reaction types. The patient presenting a deep stupor reaction and persistent preoccupation, with suicidal trends, responded with definite improvement for a period of two weeks, followed by gradual relapse, although not to the same low level as existed prior to narcosis treatment. The remaining patient, who presented an acute excitement in a predominantly manic-depressive, manic picture, failed to show any improvement following narcosis therapy. Sodium amytal was used exclusively as the narcotizing agent. The question as to the specific action of barbituric acid derivatives, as opposed to a general effect of a prolonged period of narcosis, however produced, must remain unanswered until prolonged narcosis is obtained by other drugs. Whatever the fundamental mechanisms underlying narcosis therapy may be, and despite our lack of accurate knowledge of them today, a sufficiently close temporal approximation is noted between treatment and response to warrant the assumption of a causal relationship, as opposed to merely coincidental improvement, or improvement associated with the normal course of recovery from the illness, and to sustain the feeling that, in the treatment of selected psychotic states, prolonged narcosis therapy has a definite value.

Southwestern Medicine, Phoenix, Ariz.

20: 367-408 (Oct.) 1936

Management of Intrathoracic Goiter. J. W. Hendrick, Dallas, Texas.—p. 367.

Recent Advances in Otology: Petrositis, Facial Nerve Surgery, Cochlear Tone Localization. R. C. Martin, San Francisco.—p. 371.

*Indications for Open Operation in Fractures. B. L. Schoolfield, Dallas, Texas.—p. 374.

Ocular Changes from Central Nervous System Syphilis and Administration of Tryparsamide. F. C. Cordes, San Francisco.—p. 377.

Dinitrophenol Cataract. H. F. Whalman, Los Angeles.—p. 381.

Laboratory Aids in Diagnosis of Enteric Infections. M. Greenfield, Santa Fe, N. M.—p. 385.

Indications for Open Operation in Fractures.—Schoolfield gives the following indications for open operation: fractures that cannot otherwise be replaced and maintained or cases in which too much loss of time would be occasioned by conservative methods, interposition of soft parts between fragments, or small isolated fragments that have not united, in all likelihood will not unite and are not essential to good function, nonunion and malunion. Of the fractures requiring open reduction, transverse fracture of the patella is a preeminent example. Wide separation of the fragments usually results

from the strong pull of the quadriceps group. Open reduction should be the rule in such circumstances. Fractures of the olecranon will often show more rapid and definite results with open fixation, though much will depend on the amount of separation of the fragments. Fractures about the distal end of the humerus will often require open reduction and fixation. The humerus, femur, radius, ulna and even the tibia are often the seat of fractures that do not lend themselves to sustained reduction. This may be due to the obliquity, the presence of unmanageable, sharp-pointed spicules or other mechanical difficulty, aided and abetted by marked muscular spasm. Open reductions are especially demanded in fractures neglected for days or weeks. Open reduction and fixation should be considered in the transverse fracture of the posterior part of the os calcis with its natural tendency to upward displacement because of the pull of the calf muscles.

Surgery, Gynecology and Obstetrics, Chicago

63: 417-560 (Oct.) 1936

Pathologic Physiology of Stone in Common Bile Duct: Clinical and Surgical Significance. W. Walters, Rochester, Minn.—p. 417.
*Toxemia of Pregnancy. J. R. Goodall, Montreal.—p. 425.
Appendicitis in the Small Hospital: Critical Analysis and Discussion. R. F. Sengstacken, New York.—p. 438.
Duplication of Congenital Malformations in Brothers and Sisters and Among Other Relatives: Study of Sibling Defects in Forty Consecutive Families. D. P. Murphy, Philadelphia.—p. 443.
Clinical Studies on Influence of Certain Drugs in Relation to Biliary Pain and to Variations in Intrabiliary Pressure. W. L. Butsch, J. M. McGowan and W. Walters, Rochester, Minn.—p. 451.
Three Hundred Mixed Tumors of Salivary Glands, of Which Sixty-Nine Recurred. J. McFarland, Philadelphia.—p. 457.
Surgical Treatment of Tumors of Mediastinum. W. D. Andrus and G. J. Heuer, New York.—p. 469.
Repair of Cleft Palates Primarily Unsuccessfully Operated on. E. C. Padgett, Kansas City, Mo.—p. 483.
Simple Method of Amputating Exteriorized Bowel with Carr Hilar Lobectomy Clamp: Modified Second Stage Mikulicz Operation. W. L. Wolfson and R. E. Rothenberg, Brooklyn.—p. 497.
Fixation of Fractures of Neck of Femur by Introduction of Kirschner Wires. F. G. Dyas and L. J. Aries, Chicago.—p. 499.
*Conservative Surgical Treatment of Carcinoma of Penis: Technic for Partial Amputation. R. M. Nesbit and W. A. Keitzer, Ann Arbor, Mich.—p. 504.
Treatment of Fractures of Os Calcis by Pin Traction: Study of End Results. W. R. MacAusland, Boston.—p. 506.
*Treatment of Trichomonas Vaginalis and Trichomonas in Male. E. L. Cornell and L. W. Riba, Chicago.—p. 511.
Further Observations on Treatment of Fracture Dislocations of Cervical Spine with Skeletal Traction. W. G. Crutchfield, Richmond, Va.—p. 513.
Fractures of Condyles of Tibia. E. H. Caldwell, New York.—p. 518.
Large Bowel Obstruction. R. V. B. Shier, Toronto.—p. 523.

Toxemia of Pregnancy.—Goodall considers that there is but one toxemia of pregnancy in the third trimester but that it has a very protean symptomatology. The reason for this lies in the idiosyncrasies of the patients and in the susceptibilities and reserves of systems and of individual organs to a common toxicity which bathes all the tissues generally and commonly. Susceptibility to eclampsia varies in different patients. It is important to recognize this factor, as it frequently determines the course of the disease. In the child-mothers the susceptibility to eclampsia is high, owing to instability of their nervous systems. Many women, though chronologically mature, are infantile in nerve development and instability and as such are as susceptible as children to the convulsive expression of toxemia, when from their years one might expect a milder form of reaction. The blood pressure in the early months of pregnancy ranges between 30 and 60 diastolic and between 60 and 90 systolic. It slowly rises in the third trimester under normal conditions but should not exceed from 70/100 to 80/110. In abnormal states, blood pressure begins to rise and may reach very high registration throughout the later months. In the third trimester, high maternal blood pressure leads to grave placental disease and coincidentally grave fetal circulatory disturbances. High blood pressures are commonly associated with progressive placental edema, deposition and sclerosis. Toxemia does not affect the placenta in this manner. Toxemia produces placental hemorrhages and placentosis. Retroplacental and intraplacental hemorrhages are found principally in true toxemic cases and usually in the low grade types of toxemia, cumulative and of long standing, but rarely with a blood pressure greater than 125 systolic. Placentosis and its final expression, massive death of the placenta, is found in the acute true toxemias. The vast majority of cases of clinical toxemia have no symptoms, and the only signs are a progressive pallor and an intractably rising blood pressure. These are not cases of uncomplicated toxemia. They are toxemic cases only possibly in a secondary way. But primarily the blood pressure arises out of dyscrasias other than those due to pregnancy. They constitute the great majority of the patients who have persistence of high blood pressure after delivery and eventuate after some years into chronic cardiovascular-renal cases. In such cases pregnancy is merely an incidental association, not without its influence on the primary disease and not always a baneful associate.

Surgical Treatment of Carcinoma of Penis.—Nesbit and Keitzer agree with Dean and Campbell that a lesion involving less than the distal half of the penis should have simple amputation from 1.5 to 2 cm. proximal to the involved portion. In cases in which there are regional metastases, gland dissection should be done at a later date if deemed advisable. The authors' technic of local amputation is as follows: After sterile preparation of the patient, the glans, with the lesion, is wrapped in sterile gauze to avoid contamination of the wound. A circular skin incision is made about the penis, from 1.5 to 2 cm. proximal to the involvement. The skin is bluntly dissected toward the base for a short distance and the dorsal vessels are ligated. The ventral aspect of the organ is now brought into view and the corpus spongiosum is incised at the level of the original skin incision. A number 20 F. catheter is inserted into the urethra to be used as a guide during the dissection of the corpus spongiosum from the corpora cavernosa. If the line of cleavage is found, the procedure is relatively easy; otherwise one must avoid injury to the spongy body and urethra by sharp dissection within the adjoining capsules of the corpora cavernosa. The corpora cavernosa are transected 1.5 cm. above the level of the corpus spongiosum. The cavernous arteries are ligated. Two heavy chromic mattress sutures are placed horizontally through the entire thickness of the corpora cavernosa. These sutures shape the distal end of the stump. Four vertical sutures through the corpora cavernosa capsule bring the stump to a conical shape. A suture tacks the corpus spongiosum over the rounded end, bringing the urethra out the midpoint with 1 to 1.5 cm. projecting beyond the end of the stump. The skin is trimmed to fit the stump and closed on a horizontal line with interrupted silk sutures. The importance of allowing the corpus spongiosum to project beyond the stump cannot be overemphasized. The retraction that always occurs provides a normally functioning meatus, which projects a millimeter or two and allows the free passage of a normal urinary stream. Failure to allow for this retraction results in either stricture or retraction of the meatus, or both. Petrolatum gauze dressings are applied and changed daily. The catheter is left in until the skin sutures are removed. The end result is a well shaped and satisfactory urinary and sexual organ.

Treatment of Trichomonas in Male.—During the last seven years, thirty cases of male Trichomonas infections have been observed in clinical and private practice by Cornell and Riba. It is their impression that the Trichomonas infection in the male is acquired solely through sexual contact. There may be no symptoms. Usually symptoms of chronic prostatitis are present. A urethral discharge is present when the urethra is involved. Examination of fresh urethral and prostatic secretions or urinary sediment with the microscope will reveal the motile organisms. In general, the same principles of treatment have been used as in other nonspecific infections of the lower part of the urinary tract in males. Prostatic massages and urethral and deep instillations have caused a disappearance of Trichomonas in all cases that were treated adequately and followed up. Five cases of Trichomonas prostatovesiculitis were complicated with multiple strictures of the anterior urethra. The damaged urethra may be a factor in paving the way for Trichomonas infections. Three of the wives who have been examined harbored Trichomonas in the vagina. When urethral strictures are found, they should be eradicated if possible. Weak acriflavine base solution (1:2,000) has been the most useful drug in clearing up the urethral infections.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2: 745-792 (Oct. 17) 1936

Delirious States. B. Hart.—p. 745.
Pulmonary Tuberculosis and Pregnancy. J. Young.—p. 749.
Id. H. Cohen.—p. 751.
Etiologic Relation of Streptococcus Haemolyticus to "Rheumatic" Diseases. W. Goldie and G. J. Griffiths.—p. 755.
Measurement of Muscle Tonus. J. D. O. Kerr and L. D. W. Scott. —p. 758.

Journal of State Medicine, London

44: 559-620 (Oct.) 1936

Local Authorities and Cancer, with Especial Reference to the Bradford Scheme. F. E. Chester-Williams.—p. 559.
Some Considerations for Closer Coordination of Work of the Health Officer and the Medical Profession. C. E. Goddard.—p. 575.
Observations on Health and Safety in the Factory. A. Massey.—p. 580.
*Errors in Average English Dietary Exposed by Pregnancy. G. W. Theobald.—p. 587.
English Dysenteric Infections. A. F. Hurst.—p. 598.

Errors in Average English Dietary Exposed by Pregnancy.—Theobald advances the hypothesis that all the toxemias of pregnancy, including the pyelitis of pregnancy and puerperal insanity, are caused by deficiencies in the diet. The earliest manifestation of the toxemias of pregnancy is the onset of one or more of the following symptoms: insomnia, headaches, cramps and vomiting. These symptoms, in the absence of some definite cause, arise as the result of disturbance of the calcium metabolism. The dietetic deficiency hypothesis differs fundamentally from all the other hypotheses that have been advanced to explain the etiology of the toxemias of pregnancy. Not only does it correlate all the toxemias of pregnancy but it implies that there is no essential etiologic difference between ordinary morning sickness and the decay of teeth associated with pregnancy on the one hand and eclampsia on the other. All recent surveys of the dietaries of the people of England have shown that the average individual in the islands is inadequately fed. Secondary anemia is much too prevalent among the women in this country. The author has suggested that every school throughout the country should instruct girls to take iron for one month in the year. The other substances of which pregnancy teaches that there is all too frequently an inadequate intake are vitamins A, B and D and iodine.

Lancet, London

2: 833-892 (Oct. 10) 1936

Infections of Fingers and Hand. R. M. Handfield-Jones.—p. 833.
Cross-Infection with Hemolytic Streptococci in Otorhinologic Wards. C. C. Okell and S. D. Elliott.—p. 836.
Impairment of Anterior Pituitary Functions by Follicular Hormone. B. Zondek.—p. 842.
Experimental Production of Sarcoma with Thorotrast. F. R. Selbie. —p. 847.
*Treatment of Asthmatic Attacks by Inhalation of Adrenalin. N. A. Nielsen.—p. 848.
Acholuric Jaundice in the Adult. M. Kremer and W. H. Mason. —p. 849.

Treatment of Asthmatic Attacks.—Nielsen treated more than 400 attacks of asthma in forty patients with inhalation of a 10 per cent solution of epinephrine, nebulized in the triplex or asthminhal spray. The dose may be expressed in milligrams, each compression of the ball of the triplex spray (side tube) nebulizing an amount of the solution corresponding to one-twelfth mg. of epinephrine, each compression of the asthminhal spray corresponding to one-eighteenth mg. The dose has varied between one-sixth and 1 mg., most often being from 0.5 to 0.75 mg. In all cases the treatment was very successful. The effect appears almost immediately. In slight attacks the respiration is eased after a few inhalations of the solution, and half a minute after the end of the inhalation the respiration is no longer sibilant and the rhonchi have disappeared. In a case of status asthmaticus, in which subcutaneous injection of 1 mg. of epinephrine had been without effect, the condition improved considerably on inhalation. It is difficult to determine the duration of the effect obtained. In a few cases, when the patients were in status asthmaticus, the effect seems to have lasted a fairly short time, though seldom less than an hour; in one case, however, it was only ten minutes. No change in sensitivity toward epinephrine was observed. The patients have not complained of palpitations or other subjective symptoms. One patient inhaled 1 mg. of epinephrine twelve times at intervals of an hour without any inconvenience. The favorable result is considered to be due to a local effect of epinephrine.

Medical Journal of Australia, Sydney

2: 415-446 (Sept. 26) 1936

Treatment of Chronic Arthritis. A. H. à Court.—p. 415.
Treatment of Osteo-Arthritis and Rheumatoid Arthritis. A. L. Ducker. —p. 418.
Medical Practice During Goldfields Era in Victoria. E. A. Mackay. —p. 421.
Contribution to Technic of Bronchography, with Description of New Type of Introducer for Intratracheal Catheterization. J. O'Sullivan. —p. 428.
*Investigation into Thick Blood Drop Method of Diagnosis in Leprosy. T. M. Clouston.—p. 430.

2: 447-480 (Oct. 3) 1936

Fibrositis: Treatment by Physical Means. F. May.—p. 447.
Gas Anesthesia in a Melbourne Public Hospital, 1931-1936. G. Kaye. —p. 458.

Thick Blood Drop Method of Diagnosis in Leprosy.—In performing Clouston's procedure the first drop of blood taken from an apparently well finger or thumb is wiped away and then another drop is taken and a thick drop preparation is made. This is then dried in air, under glass covers, dehemoglobinized in distilled water and again dried as before. The film is then stained by the Ziehl-Neelsen method, 5 per cent sulfuric acid being used for decolorization. Counterstaining is carried out with aqueous methylthionine chloride for three minutes. To test the efficacy of the method employed, eighteen nodular cases were investigated; acid-fast bacilli were found in skin sections and nasal smears in all. Fourteen cases showed acid-fast bacilli in the thick blood drop preparation. In the majority of the preparations acid-fast bacilli were abundant, being present both singly and in clumps and many being intracellular. In addition to the nodular cases, the blood of thirty-six patients in segregation with milder cutaneous leprosy was examined. Acid-fast bacilli were found after prolonged search in only two cases. Blood films from twenty-one persons attending the outpatient clinic were also examined. No evidence of Microbacterium leprae was found in any of these films. The patients from whom these films were taken had all suffered from neural leprosy, their infections were all clinically inactive and the examination of skin sections and nasal smears within the last two years has given negative results, eighteen having given negative results within the last nine months. Ten suspected patients were also examined with negative results. These were patients having a small area of hypopigmentation, not necessarily, though usually, associated with anesthesia or analgesia and with no acid-fast bacilli in skin section or nasal smear. Negative results were obtained with eight children whose ages ranged from 6 to 10 years, born in the leper station of leper mothers. The results of this investigation support the conclusions reached by Lowe in India. The technic is not suitable for early or latent cases of leprosy.

Journal of Oriental Med., Dairen, South Manchuria

25: 49-60 (Sept.) 1936

Pathologic-Anatomic Studies of Kaschin-Beck's Disease. M. Aiiso and N. Hayashi.—p. 49.
Quantity of Iron Contained in Blood in Kaschin-Beck's Disease. M. Aiiso and N. Hayashi.—p. 52.
Value of Sorghum-Hirse as a Vitamin C Free Diet, and Experimental Scurvy of Guinea-Pigs. M. Sugiura.—p. 53.
Reducing Substances in Malt of Soya Beans Produced in Manchuria. M. Sugiura.—p. 54.
Syphilis Transmitted by Blood Transfusion. K. Tasaki.—p. 54.
Report on Suppuration After Aseptic Operation. T. Nakajima.—p. 55.
Liver Cirrhosis Due to Congenital Obliteration of Choledochus: Case. G. Ishiyama.—p. 56.
Method of Extracting Acid-Fastness from Acid-Fast Bacilli (Bromide-Gas Method). T. Hashimoto.—p. 57.
Surgically Extirpated Splenomegaly in Manchuria. S. Hayashi.—p. 57.
Cultivation of Tubercle Bacilli: Part I. Method of Isolation of Tubercle Bacilli by Means of Gas Producing. H. Tsubosaki and H. Inoue. —p. 58.
Demonstration of Virus of Spotted Fever (R. Exanthematofebri) in Sections from Various Organs of the Rat. R. Okamoto and S. Masayama. —p. 59.

Bulletin de l'Académie de Médecine, Paris

116: 215-248 (Oct. 20) 1936

Mortality of Children Aged from 5 to 15 Years. A. Loir and H. Legangneux.—p. 219.
Vaccination Against Yellow Fever with Laigret's Vaccine. C. Mathis, C. Durieux and M. Mathis.—p. 226.
*Prognostic Value of Bactericidal Power of Serum in Pulmonary Tuberculosis. P. Courmont and H. Gardère.—p. 238.
*Cholesterol and Methylated Antigen Associated in Treatment of Tuberculosis. F. Barbary.—p. 242.

Bactericidal Power of Serum in Tuberculosis.—Courmont and Gardère report observations on the prognostic value of the bactericidal action of serum in pulmonary tuberculosis. Previously they described how in vitro tests of the bactericidal power of serum to homogeneous liquid cultures of the tubercle bacilli could be performed. Culture growth could be stimulated or inhibited by the addition of the serum removed from certain tuberculous patients. The method in brief involves the use of four tubes of culture medium with definitely measured proportions of bacilli and serum. The forty cases studied in this report were taken from persons with active tuberculous lesions. The blood was drawn during the first days of hospitalization and before any treatment had been instituted. Eleven of these patients had a weak bactericidal power and five of these died. The other twenty-nine patients showed a strong bactericidal power of the serum and only four died. Thus, among the group of patients showing the weak bactericidal power of the serum, 45 per cent died, while only 13 per cent of those with a strong bactericidal serum died. They concluded from these and previously published results that investigation of the bactericidal power of the serum can be of some prognostic value in pulmonary tuberculosis. From the standpoint of general pathology these facts are important: it seems logical to believe that increase in the bactericidal power of the blood of certain animals almost entirely refractory to tuberculosis and the elevation of bactericidal power of the blood of tuberculous persons are excellent signs of general resistance.

Cholesterol and Methylated Antigen in Treatment of Tuberculosis.—Barbary adopted a preparation consisting of 0.05 cc. of benzyl cinnamate, 0.1 cc. of pure cholesterol, 0.125 cc. of camphor and 5 cc. of pure olive oil washed with alcohol in the treatment of tuberculosis. One ampule containing 5 Gm. of this solution and 0.5 or 1 Gm. of the dilute methylated antigen of the Pasteur Institute and, finally, another ampule of the prepared solution were aspirated into a 10 cc. syringe. The mixture was then injected subcutaneously but extremely slowly. For the first two weeks the injections were made twice a week. On each intervening day two ampules of the cholesterol solution without the antigen were injected. Following this course of treatment there was a week of rest. For the succeeding two weeks the same technic was repeated but the amount of antigen doubled. The procedure was continued as long as necessary. There were no reactions, no shock and no interruption of daily occupation from this method of treatment. It is applicable in different forms of tuberculosis, including the pulmonary, osseous, cutaneous and ganglionic, and is effective in adults as well as children. The results were slow with some and fast with others but were evidenced by an arrested evolution of the process, drop in temperature, increase in weight and a more or less active regression of the lesions.

Presse Médicale, Paris

44: 1681-1704 (Oct. 28) 1936

*Hemostatic and Coagulant Effects of Primary Octylic Alcohol on Hemorrhagic Syndromes. A. Clerc, J. Sterne, J. Delamare and R. Paris.—p. 1681.
Carbolated Antirabic Vaccines: Italian Method of Treatment of Rabies. P. Remlinger and J. Bailly.—p. 1682.
Late Results of Albee's Operation for Pott's Disease of Adult. G. Leclerc.—p. 1684.

Hemostatic Effects of Octylic Alcohol.—Clerc and his colleagues state that previous work has demonstrated that bodies which lower superficial tension exert a coagulating action on the blood. This action can be demonstrated by simple mixtures in vitro, but it is even more marked following intravenous injection in the dog. They report ten cases, in all of which hemorrhagic states existed from various causes, treated in the attempt to increase the coagulability of the blood. The preparation used consisted of a pure octylic alcohol in 10 per cent ethyl alcohol, the eventual titer being about 1:1,000. Fifteen cubic centimeters of this solution was injected slowly into the vein. The coagulation time was taken from the vein of the opposite arm immediately before and fifteen minutes after the injection. Bleeding time was also determined by the classic method of Dukes. The most important result of these experiments was the definite harmlessness of the method. The coagulation time was found shortened in eight of nine patients. This was effected with great rapidity. The degree, however, varied from case to case. The duration varied widely but was observed to last from about seven days to eight weeks. The bleeding time seemed to be little modified. The clinical results were favorably influenced and there was a tendency for hemorrhages to disappear. The mode of action remains obscure. Because of the innocuousness of the procedure it can be tried without risk in any case of hemorrhagic state. While further investigation is necessary, these preliminary results are encouraging.

Clinica Medica Italiana, Milan

67: 655-726 (Oct.) 1936

Roentgen Differential Diagnosis of Aortitis. R. Avegno.—p. 657.
Diffuse Sarcoma of Stomach: Classification. L. Loi.—p. 678.
*Alterations of Structures at Base of Cranium in Lipoid Nephrosis. G. Barbaro-Forleo.—p. 696.
Behavior of Glycemia in Acute Inflammation of Lung. A. Bologna and G. C. Sironi.—p. 705.

Changes in Structures at Base of Cranium in Lipoid Nephrosis.—Barbaro-Forleo reports two cases of lipoid nephrosis. The roentgen examination of the structures at the base of the cranium showed the presence of sphenoid sinusitis, perisinusitis of the nearby sinuses and anatomic changes of the structures of the thalamo-encephalohypophyseal region. The author believes that lipoid nephrosis originates in dysfunctional disturbances of the hypophysis and the thalamo-encephalon. He advises x-ray examination of the base of the cranium in other cases of lipoid nephrosis and, if possible, anatomopathologic studies of the hypophysis and diencephalon in necropsies made on cadavers of persons who suffered from lipoid nephrosis.

Riforma Medica, Naples

52: 1471-1504 (Oct. 31) 1936

Formation of Free Bodies in Hernial Sac: Cases. I. Scalone.—p. 1471.
Postapnoic Curve in Voluntary Apnea: Diagnostic Value. V. Gambini.—p. 1472.
*D'Amato Sign for Diagnosis of Pleural Effusion. A. Sacchetti.—p. 1476.

Diagnosis of Pleural Effusion.—The D'Amato sign for diagnosis of pleural effusion consists in the change of dulness from the vertebral column to the cardiac area for displacement of pleural fluid from the posterior to the anterior costomediastinal sinus during postural changes of the patient. The sign was described by the author in the *Riforma medica* **51:**1503 (Oct. 5) 1935 and abstracted in THE JOURNAL Dec. 28, 1935, page 2190. Sacchetti investigated the sign in a great number of cases. His results confirm those of D'Amato with respect to the value of the sign in diagnosis of pleural effusion. The author advises resorting to the sign, which he considers easy to determine and as valuable as Maragliano and Grocco's signs, for the diagnosis of pleural effusion and for the differential diagnosis of several diseases of the respiratory tract.

Brasil-Medico, Rio de Janeiro

50: 991-1012 (Nov. 14) 1936

*Alkali Reserve in Tuberculosis. A. Baer Bahia.—p. 991.
Adenofibroma of Trachea: Case. T. Falcão.—p. 996.
Diagnosis of Leprosy in Santos: Work in Ambulatory Gaffrée e Guinle. A. Gonçalves de Castro Cerqueira.—p. 998.
Prevention of Tuberculosis. J. R. Da C. Doria.—p. 1000.

Alkali Reserve in Tuberculosis.—Baer Bahia says that acidosis is one of the most frequent complications of tuberculosis. Whether acidosis precedes the development of tuberculosis or is caused by it is not known. In tuberculous acidosis a vicious circle is established. Acidosis retards the processes of organic combustions and this retardation increases the acidity of the body fluids. Administration of tuberculin induces modifications in the acid base equilibrium. Patients with a low alkali reserve show an intolerance to tuberculin, which is manifested by tachycardia and loss of weight. Patients with a

normal or slightly increased alkali reserve show a relative bradycardia and increase in weight after the administration of tuberculin. Gold salts administered to tuberculous patients induce a decrease in the alkali reserve which oscillates between 10 and 20 per cent. The decrease of the alkali reserve in these cases is independent of the dose of gold salts injected provided it does not surpass from 0.25 to 0.1 Gm. of the salt. A decrease in alkali reserve is produced immediately after the injection and lasts about three hours and a half. In cases of intolerance to gold salts the use of sodium bicarbonate or citrate controls intolerance. The study of the physiology of the acid base equilibrium in tuberculosis shows the importance of metabolic disturbances in the beginning and development of tuberculosis. The latter is an infection, but its development depends on special dysergic conditions of the patient.

Revista Médica Cubana, Habana

47: 1103-1208 (Nov.) 1936

*Does Function of Diaphragm Return in Phrenicectomized Patients? R. M. Boza Mesa.—p. 1103.
Infantile Hysteria Cured by Psychoanalysis. B. Cardelle y Penichet and L. Muñiz Angulo.—p. 1125.

The Diaphragm in Phrenicectomized Patients.—Boza Mesa states as a fact that the diaphragm resumes its function after phrenicectomy. He followed the evolution of paralysis in a group of eight patients and found that in all cases the collapse of the lung was successfully obtained and the mobility and functions of the diaphragm were reestablished within one and five years after phrenicectomy. The several hypotheses given in the literature as an explanation for the resumption of diaphragmatic functions are supplementary innervation by the phrenic nerve of the opposite side to that on which phrenicectomy was done, and innervation from the intercostal, subclavian or accessory phrenic nerves or else by sympathetic fibrils. The author's report confirms the reports in the literature on the reestablishment of diaphragmatic function after phrenicectomy and the time in which the function is resumed. The mechanism by which mobility and function of the diaphragm are reestablished depends on certain factors not yet determined.

Semana Médica, Buenos Aires

43: 1249-1320 (Nov. 5) 1936. Partial Index

Excretion Urography. H. D. Berri.—p. 1249.
Transplantation of Bovine Hypophysis in Human Beings. C. P. Waldorp, J. Reforzo Membrives and S. E. Luchetti.—p. 1277.
*Adiposogenital Dystrophy from Late Syphilis: Case. J. B. Galand. —p. 1288.
Acute Edema of Lung in Mitral Stenosis and Insufficiency: Case. D. Boccia.—p. 1296.
Pregnancy and Pernicious Anemia. M. Mordeglia and E. Terán Piedrabuena.—p. 1302.
Fibromyxoma of Abdominal Wall: Case. R. Pini and M. Nicastro. —p. 1307.

Adiposogenital Dystrophy from Late Syphilis.—In the case reported by Galand a man, aged 69, acquired syphilis at 23 and was insufficiently treated. Some time later he married and had two children. At the age of 38 he suffered from a semigeneralized alopecia, which left only a small amount of hair on his head. This was followed soon by the establishment of excessive thirst, polyuria, feminine obesity, diabetes insipidus and a typical Fröhlich syndrome. The condition lasted ten years, at the end of which time he was given antisyphilitic treatment, which controlled obesity and diabetes and started regrowth of the hair. The treatment, however, had no effect on the sexual disturbance. A diagnosis of adiposogenital dystrophy from late syphilis was made. The blood changes (oligocythemia, oligochromemia and mononucleosis), the presence of metabolic disturbances and the conservation of a clear mind, which are characteristic properties of adiposogenital dystrophy, were present in the patient's case. The syphilitic etiology is undoubted. Roentgen studies of the skull and of the sella turcica showed normal structures, but the functions of the hypophysis could not be evaluated. The author believes that the adiposogenital dystrophy developed from functional disturbances of the hypophysis by a syphilitic gumma located in the hypophyseal region or by a syphilitic meningo-encephalitic process. His opinion is based on the previous existence of obesity and diabetes (two conditions that originate in functional hypophyseal disturbances), the previous existence of thirst and polyuria (two conditions that originate in anatomic changes of the hypothalamus) and the satisfactory results of antisyphilitic treatment in controlling these disturbances.

Medizinische Welt, Berlin

10: 1537-1572 (Oct. 24) 1936. Partial Index

Is Meat Diet Unnecessary and Harmful? P. Schenk.—p. 1537.
Diurnal Rhythms in Their Significance for Hormone Therapy. A. Jores. —p. 1542.
How to Recognize and Overcome Resistance in Treatment of Neuroses. O. Kant.—p. 1545.
*Carcinoma on Basis of Endometriosis. E. Vogt.—p. 1548.
Diseases of Urinary Organs During Pregnancy. O. Wolf.—p. 1550.

Carcinoma on Basis of Endometriosis.—Vogt, after reviewing a case that was described by Hanser, reports a case of his own. The patient, a woman now 53 years of age, underwent roentgen castration at the age of 35 on account of severe hemorrhages. There were recurrences of the hemorrhages, which were counteracted by repeated irradiations. In August 1935 the patient was again hospitalized on account of severe hemorrhages and this time the uterus was removed by an abdominal radical operation. The recovery was uneventful, but after ten months the woman complained of a downward pressure, backache and a peculiar sensation in the rectum. The examination revealed nodular thickening of the posterior vaginal wall below the scar and a tough, irregular infiltration in the entire rectovaginal septum. The histologic examination of a nodule of the posterior vaginal wall disclosed a carcinoma on the basis of a benign endometriosis.

Monatsschrift f. Geburtshülfe u. Gynäkologie, Berlin

103: 185-304 (Oct.) 1936. Partial Index

Estrogenic Hormone as Sex Specific Growth Hormone and Its Relation to General Growth Hormone. L. Seitz.—p. 185.
Problems in Operation of Genital Prolapse. A. Mayer.—p. 194.
Method of and Indications for Cesarean Delivery. R. T. von Jaschke. —p. 198.
*Reexamination and Simplification of Pregnancy Reaction According to Visscher and Bowman. B. Friedrich.—p. 211.
Bactericidal Action of Blood in Puerperal Fever and Cervical Carcinoma. F. Daels.—p. 217.

Modification of Pregnancy Reaction According to Visscher and Bowman.—Friedrich directs attention to the chemical pregnancy reaction of Visscher and Bowman (*Deutsche med. Wchnschr.* **60:**1837 [Nov. 30] 1934; abstr. THE JOURNAL, Feb. 2, 1935, p. 431). Numerous experiments and modifications convinced him that the outcome of the reaction is chiefly determined by the hydrochloric acid. Methyl cyanide and hydrogen dioxide seem to be least involved in the reaction, and phenylhydrazine hydrochloride gives the fluid the basic yellow color. If these three reagents are omitted, the color changes only from yellowish brown to brown. However, if these three reagents are used and only hydrochloric acid is omitted, there is no reaction whatever. To prove that the gonad-stimulating factor is the only hormone which, when treated with hydrochloric acid, produces a color reaction, the author tested a number of other hormone preparations. He found that, aside from slight turbidities produced by thyroxine and insulin, the gonad-stimulating factor remains the only hormone which, when heated with hydrochloric acid, gives a strong color reaction with a rather coarse precipitate. The same 312 urine specimens, which he examined according to the technic of Visscher and Bowman, he examined also according to two methods devised by himself. In the first he added to 1 cc. of urine, the specific gravity of which had been brought to 1.015, 3 drops of a 25 per cent solution of hydrochloric acid and heated this mixture for twenty-five minutes in a boiling water bath. A clear, permeable light brown fluid without a precipitate indicates a negative reaction, but the test is positive if the urine is reddish brown or a dark brown and if a precipitate makes it turbid. In the second method 5 drops of a 25 per cent solution of hydrochloric acid are added to 1 cc. of urine (specific gravity of 1.015). Then the mixture is heated to the boiling point for exactly two minutes over the Bunsen burner. A light brown indicates a negative reaction; a reddish brown or dark brown a positive reaction. A precipitate is usually absent with this technic. Only five contradictory results were obtained in the 312 specimens of urine (tested with the Visscher-Bowman and the author's technics). The hydrochloric acid method gave the correct results in these five cases.

Zentralblatt für Chirurgie, Leipzig

63: 2593-2640 (Oct. 31) 1936

*Arteriographic Presentation of Injuries of Cerebral Vessels. W. Löhr. —p. 2359.
Newer Methods of Treatment in Cases of Prostatic Disease in Which Operations Cannot be Performed. O. Henningsen.—p. 2608.
Types of Splints for Transport of Fractures. M. Tiegel.—p. 2612.
Surgical Treatment of Trophoneurotic Decubitus Ulcers of Feet. A. N. Popovici, M. V. Ghimpetzeanu, A. Valeanu and G. Georgescu.—p. 2617.
Hemolytic Icterus Cured by Splenectomy: Case. F. Dobos and J. Erdély.—p. 2619.

Injuries of Cerebral Vessels.—Löhr cites cases treated at the surgical clinic of the State Hospital of Magdeburg-Altstadt in which demonstration and localization of thrombosis or injury to one of the larger cerebral vessels was made possible by arteriography. The author has in mind cases of severe injury to brain tissue presenting complicated neurologic symptoms and an indefinite history. It is here that arteriography is capable of rendering service in establishing a diagnosis and permitting more active treatment. This is particularly true of hemorrhages from the epidural or subdural vessels, since it is this type of case that constitutes the most frequent indication for surgical intervention in order to relieve the classic symptoms of increased intracranial pressure. Experience with surgery of brain tumors as well as that with hemorrhagic pachymeningitis demonstrates that, besides the purely mechanical effect, bleeding is capable of producing a toxic effect as well. The author likewise calls attention to the fact that the conservative method of lumbar puncture is not always a safe procedure in the severe cases complicated by swelling of the brain. The surgeon's problem is to be able to select from the cases of brain injury those due to bleeding and, when possible, to aid them by the removal of blood clots or by arresting the bleeding. Arteriography constitutes the most reliable method for localization of the bleeding. The method is indicated in cases of skull and brain injury in which the history and the neurologic examination fail to establish an accurate diagnosis of epidural or subdural hemorrhage.

Polska Gazeta Lekarska, Lwów

15: 845-864 (Nov. 1) 1936

Anomalous Division of Cells and Its Influence on Development of Some Individual Characteristics. J. Alexandrowicz.—p. 845.
Investigations on Acute Form of Tuberculosis Among Rabbits: So-Called Tuberculosis of Yersin Type. F. Van Deinse and M. A. Domański. —p. 847.
Comparative Research on Tubercle Bacilli in Immunized and Non-immunized Rabbits. T. Kielanowski and E. Lukidis.—p. 848.
Degeneration and Regeneration of Peripheral Motor Neurons: Morphologic Functional Aspect. W. S. Hołobut and B. Jałowy.—p. 849.
*Value of Microscopic Examination of Liver in Diagnosis of Death by Drowning. B. Popielski.—p. 856.

Diagnosis of Death by Drowning.—Popielski says that it is often impossible to make a diagnosis in cases of drowning. He reviews the literature and the minutes of postmortem examinations in cases of death by drowning and finds that the supposed signs, (1) excess of venous blood supply in the liver, (2) weight of the liver and (3) the dark red color, are the same symptoms that appear in cases of asphyxiation. He experimented on thirty-six animals and concluded that microscopic examination of the liver is not dependable and therefore unpractical. He summarizes his views as follows: A superfluity of venous blood in the liver has a distinct value. It always appears in cases of death by drowning and so aids in the diagnosis. This change may be verified in histologic specimens and, when other anatomic symptoms are lacking, points to death by drowning. But it is also found in asphyxiation.

Vrachebnoe Delo, Kharkov

19: 577-656 (No. 7) 1936. Partial Index

Vitality of the Heart. G. N. Nikolaev.—p. 585.
Comparative Evaluation of Water Tests for Fractional Diagnosis of Circulation. T. I. Meerzon and A. N. Berinskaya.—p. 587.
Effect of Histolysates on Take of a Transplant. F. Brikker and I. Zilbert.—p. 595.
Ultrafiltrability of Strain Neoplasms. M. F. Runova.—p. 601.
*Insulin Therapy in Pneumonia of the Aged. S. N. Sinelnikov.—p. 603.

Insulin Therapy in Pneumonia of the Aged.—Sinelnikov regards pneumonia as a state of nondiabetic pathologic acidosis running a course characterized by a pronounced anoxemia with a considerable increase in the blood sugar, increased breaking down of albumin and fat, and marked lowering of the chloride metabolism. Achard was the first to refer to insulin as an alkalinizing agent, and Kogan-Yasnyy was the first to apply it in the treatment of pneumonia. The blood sugar of the pneumonia patients was found to vary between 0.120 and 0.160 at the peak of the temperature curve. With the fall of the temperature the blood sugar content was from 0.09 to 0.08 per cent. The chlorides at the height of the disease varied between 0.58 and 0.6, during the crisis from 0.93 to 6.8, and several days after the crisis from 8.8 to 12. Insulin was administered twice daily in doses of from 0.5 to 1.5 Gm. The author reports 122 cases of croupous and of bronchial pneumonia treated by this plan without a fatality. In a specially selected group of eighteen elderly patients there was not a single fatal issue. The author reports four cases in which the insulin therapy did not prevent death. On necropsy these were shown to have been complicated respectively by carcinoma, active tuberculosis, infarct of the left lung and a ruptured aortic aneurysm.

Nederlandsch Tijdschrift voor Geneeskunde, Haarlem

80: 5289-5380 (Nov. 28) 1936. Partial Index

Pneumocephalus. W. G. Sillevis Smitt.—p. 5296.
Acceleration of Normal Delivery. H. P. A. Smit.—p. 5303.
*Local Disturbances of Autonomic Innervation Resulting from Trauma. C. T. Van Valkenburg.—p. 5311.
Pain in Shoulder. L. L. Posthuma.—p. 5317.
Unusual Case of Hyperemesis. B. Van Tricht.—p. 5319.
Venereal Mixed Chancre of Neck: Case. J. Nieuwenhuyse and P. J. Van Putte.—p. 5322.
Enlargement of Vagina and Uterus Produced by Estrogen. R. Schuurmans.—p. 5326.

Disturbances in Autonomic Innervation.—Van Valkenburg describes three cases of neurovegetative disturbances of traumatic origin. In the first case a disturbance in the sympathetic innervation of the hands and the forearms developed in a man who, as the result of a fall, held himself with his hands in order to keep from drowning until he was rescued. Following this, pain and stiffness developed in his hands and he was unable to work. An examination four months later revealed changes in the hands and lower part of the arms resembling those of acromegaly (skin cold, pasty and with red and blue spots; nails dry and brittle). Some of the fingers were bent and could not be actively stretched out; attempted passive stretching caused severe pain. The sensitivity was not impaired and the electrical irritability was likewise normal. Roentgenoscopy revealed atrophy of the hands and lower part of the arms. The condition improved in the course of time. The author is convinced that the disorders were caused by a local impairment of the sympathetic innervation, which in turn resulted from the blunt force exerted on the hands in the course of the fall. The second case concerns a man in whom trophic disturbances developed in the region of the peroneal nerve following a fracture of the tibia. In the third patient the disturbances in the sympathetic innervation developed as the result of a stroke of lightning.

Acta Medica Scandinavica, Stockholm

90: 1-314 (Oct. 7) 1936. Partial Index

*Pancreatic Secretion in Man After Intravenous Administration of Secretin. G. Ågren and H. Lagerlöf.—p. 1.
Processes of Stimulation and Inhibition of Connective Tissue. V. G. Boudyline.—p. 59.
Immediate Effect of Splenectomy on Blood Picture in Essential Thrombopenia. S. Wahlqvist.—p. 81.
Experimental and Clinical Observations on Influence of Hypophyseal and Parathyroid Preparations on Secretory and Motor Functions of Stomach. D. M. Rossiisky, J. J. Kantorovitch, J. J. Karmasine and A. A. Jouravel.—p. 151.
Standardization of Liver Extracts. J. Dedichen.—p. 195.
*Autocerebrospinal Fluid Therapy of Epidemic Cerebrospinal Meningitis of Children. J. S. Weiner and S. F. Bakkal.—p. 214.

Pancreatic Secretion in Man.—Ågren and Lagerlöf state that, although Bayliss and Starling performed their classic secretin experiments in 1902, there are still authors who express doubts as to the existence of a secretin stimulation as an integral part of normal digestion. On the basis of their experiments the authors state that it is possible to give the following picture of the effect of secretin stimulation on the digestive mechanism in man: After the intravenous injection of secretin a lively discharge of pancreatic juice sets in, usually before a minute has elapsed. The volume of secretion reaches its maximum within twenty minutes, usually within ten minutes,

the peak being followed by a rather slow decline. Parallel with the volume there is, as a most conspicuous feature, a rapid rise in the concentration of bicarbonate. The concentration first lags a little behind the volume and, after the maximal concentration has been reached, declines somewhat slower than the volume. The authors consider the dosage of secretin used in their experiments a submaximal dose. With this dose the maximal bicarbonate concentration is closely milliequivalent to the blood plasma and the gastric juice. The discharge of the pancreatic enzymes follows a somewhat different course. There is during the first ten minutes a great amount of enzymes (trypsin and diastase) excreted in the first abundant secretion of juice, an amount no doubt representing material stored in the gland before the hormone stimulation. After this sudden peak a secretion of presumably new-formed enzyme becomes apparent, about the time the bicarbonate concentration reaches its maximum. This enzyme production continues at a rather constant level for a considerable time, at a higher rate than before the secretin stimulation. As the volume of the juice diminishes the enzyme concentration increases. In normal persons after the secretin injection, bile does not appear in the duodenal content or in occasional traces only. In persons who have had their gallbladder removed but who otherwise are normal, the situation is different. Here every sample after the secretin injection is more or less heavily stained with bile. Secretin thus stimulates the flow of bile in man, a flow which in unmutilated normal persons on the whole is taken up into the gallbladder just as it is in animals. The variations in secretin response in the different individuals of the series might be considered within moderate limits, the agreement between repeated tests on the same person being close.

Autocerebrospinal Fluid Therapy of Epidemic Meningitis in Children.—Weiner and Bakkal during 1933, 1934 and 1935 treated fifty patients suffering from cerebrospinal meningitis. Seven were treated with a polyvalent meningococcus serum, nineteen by lumbar punctures and twenty-four by subcutaneous injection of the patients' own cerebrospinal fluid. The authors were impressed with the unsatisfactory results of the polyvalent vaccine therapy. The results were poorest with the method of lumbar puncture. Of the nineteen patients so treated, fifteen died. Of the twenty-four patients treated by hypodermic administration of the patients' own cerebrospinal fluid, nineteen recovered and five died. Despite the small number so treated, the authors regard this simple method of treatment as more promising than any heretofore attempted.

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79: 755-838 (Sept.) 1936

Result of Roentgen Treatment of Carcinoma of Neck of Uterus. J. J. Chydenius.—p. 755.
Attempts with Anticatarrhal Vaccine. E. Wolff.—p. 765.
*Intravenous Anesthesia with Sodium Salt of *n*-Methyl-Cyclo-Hexenyl-Methyl Barbituric Acid: Three Years' Experiences. H. E. Blomquist.—p. 773.
*Adsorption Ability of Plasma Proteins: Continued Investigations. M. C. Ehrström.—p. 802.
Blood Groups and Gonoreaction. T. Packalén.—p. 808.

Intravenous Anesthesia with *n*-Methyl-Cyclo-Hexenyl-Methyl Barbituric Acid.—On the basis of 529 cases of anesthesia with the sodium salt of *n*-methyl-cyclo-hexenyl-methyl barbituric acid from 1933 to 1936, Blomquist states that the anesthesia occurs quickly and without disagreeable sensations; there is no excitation, but more or less muscular tension not infrequently occurs, perhaps with trembling of the body for several minutes. The awakening is usually quick and pleasant. It can be given without preparation, but a prenarcotic may advantageously be used, especially in young persons. It is suitable for all operations of short duration in which there is no danger of aspiration and as the introductory anesthesia in long continued interventions, particularly where there is fear of narcosis and in psychic disturbance, and is an excellent means for weak old persons. The dosage should receive especial attention; biologic dosage is recommended. The author advises against the use of this anesthetic in cases in which there are disorders of the liver and kidneys and in greatly dehydrated persons and says that the dosage must be given with greatest care in cases of toxic injury and fever. Postnarcotic unrest is an occasional drawback, and now and then a person resistant to the agent is encountered.

Adsorption Ability of Plasma Proteins.—Ehrström says that in cachexia due to tumor, as in nephroses in the sense of nephropathies with pronounced albuminuria, the adsorption ability of the plasma proteins is lowered and likewise does not depend on a hypoproteinemia or a hypo-albuminemia. A probable explanation of the phenomenon is to be sought in the disturbed synthesis of the plasma proteins. In nephrosis the loss of albumin through the kidneys leads to a primary reduction in the blood albumin, which is eventually compensated by an increased synthesis of plasma proteins. In cachexia from tumor the hypoproteinemia occurs because of an increased breaking down or defective synthesis. In both cases the hypothesis is that the disturbed synthesis of the plasma proteins results in the formation of plasma proteins not of equal rank with the proteins in the normal system but having a defective adsorption ability.

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Sanctorius Sanctorinus: Experimental Physiologist from Beginning of Seventeenth Century; with Investigations on His Relation to Danish Medical Science, on Tercentenary of His Death. E. Gotfredsen.—p. 935.
*Hyperglobinemia with Disturbance of Central Nervous System on Toxi-Infectious Basis with Remarks on Differential Diagnosis with Regard to Myelomatosis: New Case. J. Bing, M. Fog and A. V. Neel.—p. 944.
Two Rare Lesions of Divers. N. I. Nissen.—p. 950.

Hyperglobinemia.—Bing and his co-workers have previously reported two cases characterized by marked hyperglobinemia, with resulting high blood sedimentation reaction and positive formol reaction, and extensive changes in the central nervous system, especially in the cauda equina, spinal roots and medulla, together with changes in the spinal fluid. In the case now reported, a woman aged 57, with like changes in blood and spinal fluid, there were both in the central nervous system and outside it in the various organs localized inflammatory changes with numerous lymphocytes, plasma cells and cells belonging to the reticulo-endothelial system; in the bone marrow, signs of lively cell proliferation appeared but no signs of myeloma were found. Similar changes in the blood were seen in two microscopically verified cases of myelomatosis, but in the case in which the spinal fluid was examined it was normal, and in the other in which the central nervous system was examined, no changes were found which agreed with those in the three cases of hyperglobinemia with disturbance of the central nervous system described.

98: 961-980 (Oct. 8) 1936

*Osteomalacia of Spinal Column. E. Meulengracht and A. R. Meyer.—p. 961.
*Xanthomatosis Universalis Given Roentgen Treatment: Case. P. A. Blinkenberg.—p. 968.
Fourth International Congress for Experimental Cell Research in Copenhagen, August 10 to 15, 1936. H. Okkels.—p. 972.

Osteomalacia of Spinal Column.—Meulengracht and Meyer state that in four patients, who subsisted for a long time on a one-sided diet, a disorder of the spinal column developed with osteoporosis, hour-glass deformity and breaking down of vertebrae, changes similar to those in the so-called nonpuerperal forms of osteomalacia. The factors that lead to the development of osteomalacia are assumed to have been active in these instances. Depending on the kind and degree of the causative nutritional deficiency, the changes in the spinal column may appear alone or in combination with other deficiency symptoms. A case of combination with scurvy is reported.

Roentgen Treatment of Xanthomatosis Universalis.—Blinkenberg says that in his case of universal xanthomatosis in a girl, aged 2, clinical recovery after roentgen treatment over a period of three months is manifest two years after the end of treatment. The roentgen doses were all small, so that no epilation appeared, even on the cranium, where most of the treatment was given, and treatment of such large fields with larger doses would hardly have been possible without grave effect on the whole organism. He believes that irradiation was the curative factor, because the processes in the cranium were still developing while the other affected places were being treated and did not subside until sufficient treatment had been given locally.